```
=> file reg
FILE 'REGISTRY' ENTERED AT 14:15:07 ON 17 FEB 2004
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   16 FEB 2004  HIGHEST RN 651003-77-9
DICTIONARY FILE UPDATES:  16 FEB 2004  HIGHEST RN 651003-77-9

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2003

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> e 141256-04-4
E1            1     141256-02-2/RN
E2            1     141256-03-3/RN
E3            1 --> 141256-04-4/RN
E4            1     141256-05-5/RN
E5            1     141256-06-6/RN
E6            1     141256-07-7/RN
E7            1     141256-08-8/RN
E8            1     141256-09-9/RN
E9            1     141256-10-2/RN
E10           1     141256-11-3/RN
E11           1     141256-12-4/RN
E12           1     141256-13-5/RN

=> s e3
L2            1 141256-04-4/RN

=> d rn cn

L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   141256-04-4  REGISTRY
CN   β-D-Glucopyranosiduronic acid, (3β,4α,16α)-28-[[O-D-
     apio-β-D-furanosyl-(1→3)-O-β-D-xylopyranosyl-(1→4)-
     O-6-deoxy-α-L-mannopyranosyl-(1→2)-4-O-[5-[[5-(α-L-
     arabinofuranosyloxy)-3-hydroxy-6-methyl-1-oxooctyl]oxy]-3-hydroxy-6-methyl-
     1-oxooctyl]-6-deoxy-β-D-galactopyranosyl]oxy]-16-hydroxy-23,28-
     dioxoolean-12-en-3-yl O-β-D-galactopyranosyl-(1→2)-O-[β-D-
     xylopyranosyl-(1→3)]- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Oleanane, β-D-glucopyranosiduronic acid deriv.
OTHER NAMES:
CN   QA 21
CN   QA 21V1
CN   QS 21
CN   Saponin QA 21V1
CN   Stimulon
```

```
=> => file caplus; d que l7; d que 19; d que l17
FILE 'CAPLUS' ENTERED AT 15:47:25 ON 17 FEB 2004
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```


FILE COVERS 1907 - 17 Feb 2004 VOL 140 ISS 8
FILE LAST UPDATED: 16 Feb 2004 (20040216/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L2             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  141256-04-4/RN
L3           354 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2 OR QA (W) (21 OR 21V1) OR
                 QS 21 OR SAPONIN QA
L5         20624 SEA FILE=CAPLUS ABB=ON  PLU=ON  STEROLS+PFT/CT
L6         42458 SEA FILE=CAPLUS ABB=ON  PLU=ON  VACCINES
L7             5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3 AND L5 AND L6


L4         10222 SEA FILE=CAPLUS ABB=ON  PLU=ON  SAPONINS+PFT/CT
L5         20624 SEA FILE=CAPLUS ABB=ON  PLU=ON  STEROLS+PFT/CT
L6         42458 SEA FILE=CAPLUS ABB=ON  PLU=ON  VACCINES
L9            14 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND L5 AND L6


L2             1 SEA FILE=REGISTRY ABB=ON  PLU=ON  141256-04-4/RN
L3           354 SEA FILE=CAPLUS ABB=ON  PLU=ON  L2 OR QA (W) (21 OR 21V1) OR
                 QS 21 OR SAPONIN QA
L4         10222 SEA FILE=CAPLUS ABB=ON  PLU=ON  SAPONINS+PFT/CT
L5         20624 SEA FILE=CAPLUS ABB=ON  PLU=ON  STEROLS+PFT/CT
L6         42458 SEA FILE=CAPLUS ABB=ON  PLU=ON  VACCINES
L7             5 SEA FILE=CAPLUS ABB=ON  PLU=ON  L3 AND L5 AND L6
L9            14 SEA FILE=CAPLUS ABB=ON  PLU=ON  L4 AND L5 AND L6
L11          155 SEA FILE=CAPLUS ABB=ON  PLU=ON  QUILLAJA SAPONARIA/CT
L12        88105 SEA FILE=CAPLUS ABB=ON  PLU=ON  LIPIDS, BIOLOGICAL STUDIES/CT
L15        36854 SEA FILE=CAPLUS ABB=ON  PLU=ON  VACCINES/CT
L16            7 SEA FILE=CAPLUS ABB=ON  PLU=ON  L11 AND L15 AND (L12 OR L5)
L17            3 SEA FILE=CAPLUS ABB=ON  PLU=ON  L16 NOT (L7 OR L9)

=> s l7 or l9 or l17
L68           17 L7 OR L9 OR L17
```

```
=> file medline; d que l23; d que l24
FILE 'MEDLINE' ENTERED AT 15:47:58 ON 17 FEB 2004

 FILE LAST UPDATED: 14 FEB 2004 (20040214/UP). FILE COVERS 1958 TO DATE.

 On December 14, 2003, the 2004 MeSH terms were loaded. See HELP RLOAD
 for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary. See http://www.nlm.nih.gov/mesh/ and
 http:\\www.nih.gov/pubs/yechbull/nd03/nd03_mesh.html for a description
 on changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L18             5 SEA FILE=MEDLINE ABB=ON  PLU=ON  QUILLAJA/CT
L20        112335 SEA FILE=MEDLINE ABB=ON  PLU=ON  STEROLS+NT/CT
L21          5033 SEA FILE=MEDLINE ABB=ON  PLU=ON  PHYTOSTEROLS+NT/CT
L22         91413 SEA FILE=MEDLINE ABB=ON  PLU=ON  VACCINES+NT/CT
L23             0 SEA FILE=MEDLINE ABB=ON  PLU=ON  L18 AND (L20 OR L21) AND L22


L19          4881 SEA FILE=MEDLINE ABB=ON  PLU=ON  SAPONINS+NT/CT
L20        112335 SEA FILE=MEDLINE ABB=ON  PLU=ON  STEROLS+NT/CT
L21          5033 SEA FILE=MEDLINE ABB=ON  PLU=ON  PHYTOSTEROLS+NT/CT
L22         91413 SEA FILE=MEDLINE ABB=ON  PLU=ON  VACCINES+NT/CT
L24             4 SEA FILE=MEDLINE ABB=ON  PLU=ON  L19 AND (L20 OR L21) AND L22

=> file embase
FILE 'EMBASE' ENTERED AT 15:49:10 ON 17 FEB 2004
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 FILE COVERS 1974 TO 12 Feb 2004 (20040212/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d que l30; d que l32; d que l41
L25            89 SEA FILE=EMBASE ABB=ON  PLU=ON  QUILLAJA
L27         91738 SEA FILE=EMBASE ABB=ON  PLU=ON  STEROL+NT/CT
L28           883 SEA FILE=EMBASE ABB=ON  PLU=ON  PHYTOSTEROL/CT
L29         80361 SEA FILE=EMBASE ABB=ON  PLU=ON  VACCINE+NT/CT
L30             3 SEA FILE=EMBASE ABB=ON  PLU=ON  L25 AND (L27 OR L28) AND L29


L26          4896 SEA FILE=EMBASE ABB=ON  PLU=ON  SAPONIN+NT/CT
L27         91738 SEA FILE=EMBASE ABB=ON  PLU=ON  STEROL+NT/CT
L28           883 SEA FILE=EMBASE ABB=ON  PLU=ON  PHYTOSTEROL/CT
L29         80361 SEA FILE=EMBASE ABB=ON  PLU=ON  VACCINE+NT/CT
L31            15 SEA FILE=EMBASE ABB=ON  PLU=ON  L26 AND (L27 OR L28) AND L29
L32            12 SEA FILE=EMBASE ABB=ON  PLU=ON  L31 NOT (GINSENG OR SPECTRAL
```

OR MECHANISMS)/TI

L27 91738 SEA FILE=EMBASE ABB=ON PLU=ON STEROL+NT/CT
L28 883 SEA FILE=EMBASE ABB=ON PLU=ON PHYTOSTEROL/CT
L29 80361 SEA FILE=EMBASE ABB=ON PLU=ON VACCINE+NT/CT
L34 429412 SEA FILE=EMBASE ABB=ON PLU=ON LIPID+NT/CT
L38 232 SEA FILE=EMBASE ABB=ON PLU=ON ISCOM/CT
L39 220 SEA FILE=EMBASE ABB=ON PLU=ON QS 21/CT
L41 12 SEA FILE=EMBASE ABB=ON PLU=ON L38 AND L39 AND ((L27 OR L28) OR L34) AND L29

=> s l30 or l32 or l41
L69 23 L30 OR L32 OR L41

=> file biosis
FILE 'BIOSIS' ENTERED AT 15:50:44 ON 17 FEB 2004
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 11 February 2004 (20040211/ED)

FILE RELOADED: 19 October 2003.

=> d que l51; d que l54; d que l56
L43 322 SEA FILE=BIOSIS ABB=ON PLU=ON QUILLAJA OR QS 21?
L45 145974 SEA FILE=BIOSIS ABB=ON PLU=ON ?STEROL
L46 264334 SEA FILE=BIOSIS ABB=ON PLU=ON ?LIPID
L47 112648 SEA FILE=BIOSIS ABB=ON PLU=ON ?VACCIN?
L48 441894 SEA FILE=BIOSIS ABB=ON PLU=ON IMMUNOL?
L49 12 SEA FILE=BIOSIS ABB=ON PLU=ON L43 AND (L45 OR L46) AND (L47 OR L48)
L50 5 SEA FILE=BIOSIS ABB=ON PLU=ON L49 AND (ISCOM OR ANALOG OR GUINEA)/TI
L51 4 SEA FILE=BIOSIS ABB=ON PLU=ON L50 NOT MURAMYL/TI

L43 322 SEA FILE=BIOSIS ABB=ON PLU=ON QUILLAJA OR QS 21?
L44 7733 SEA FILE=BIOSIS ABB=ON PLU=ON SAPONIN
L45 145974 SEA FILE=BIOSIS ABB=ON PLU=ON ?STEROL
L46 264334 SEA FILE=BIOSIS ABB=ON PLU=ON ?LIPID
L47 112648 SEA FILE=BIOSIS ABB=ON PLU=ON ?VACCIN?
L48 441894 SEA FILE=BIOSIS ABB=ON PLU=ON IMMUNOL?
L49 12 SEA FILE=BIOSIS ABB=ON PLU=ON L43 AND (L45 OR L46) AND (L47 OR L48)
L53 28 SEA FILE=BIOSIS ABB=ON PLU=ON L44 AND (L45 OR L46) AND (L47 OR L48) NOT L49
L54 4 SEA FILE=BIOSIS ABB=ON PLU=ON L53 AND (SAPONIN LIPID OR DETERGENT OR EMULSION OR SLIPID (3W) QS 21)/TI

L43 322 SEA FILE=BIOSIS ABB=ON PLU=ON QUILLAJA OR QS 21?

```
L44          7733 SEA FILE=BIOSIS ABB=ON  PLU=ON  SAPONIN
L45        145974 SEA FILE=BIOSIS ABB=ON  PLU=ON  ?STEROL
L46        264334 SEA FILE=BIOSIS ABB=ON  PLU=ON  ?LIPID
L47        112648 SEA FILE=BIOSIS ABB=ON  PLU=ON  ?VACCIN?
L48        441894 SEA FILE=BIOSIS ABB=ON  PLU=ON  IMMUNOL?
L49            12 SEA FILE=BIOSIS ABB=ON  PLU=ON  L43 AND (L45 OR L46) AND (L47
                  OR L48)
L53            28 SEA FILE=BIOSIS ABB=ON  PLU=ON  L44 AND (L45 OR L46) AND (L47
                  OR L48) NOT L49
L55             2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L53 AND OIL IN WATER EMULSION
L56             1 SEA FILE=BIOSIS ABB=ON  PLU=ON  L55 NOT EFFICACY/TI

=> s l51 or l54 or l56
L70             9 L51 OR L54 OR L56

=> file wpid; d que l64; d que l66; d que l67
FILE 'WPIDS' ENTERED AT 15:52:16 ON 17 FEB 2004
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FILE LAST UPDATED:          13 FEB 2004      <20040213/UP>
MOST RECENT DERWENT UPDATE:     200411        <200411/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE


>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS  <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
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 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

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    http://thomsonderwent.com/coverage/latestupdates/           <<<

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    GUIDES, PLEASE VISIT:
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    DERWENT UPDATE 200403.
    THE TIME RANGE CODE WILL ALSO CHANGE FROM 018 TO 2004.
    SDIS USING THE TIME RANGE CODE WILL NEED TO BE UPDATED.
    FOR FURTHER DETAILS: http://thomsonderwent.com/chem/polymers/ <<<



L57          128 SEA FILE=WPIDS ABB=ON  PLU=ON  QUILLAJA OR (QS OR QA)(W) 21 OR
                  QA 21V1
L59        13939 SEA FILE=WPIDS ABB=ON  PLU=ON  ?STEROL
L60        19469 SEA FILE=WPIDS ABB=ON  PLU=ON  ?LIPID
L61        19835 SEA FILE=WPIDS ABB=ON  PLU=ON  VACCIN?
L62        92215 SEA FILE=WPIDS ABB=ON  PLU=ON  IMMUN?
L63           34 SEA FILE=WPIDS ABB=ON  PLU=ON  L57 AND (L59 OR L60) AND (L61
                  OR L62)
L64           10 SEA FILE=WPIDS ABB=ON  PLU=ON  L63 AND (QS 21 OR LIPID? OR
                  STEROL OR FRACTIONAT?)/TI
```

```
L57          128 SEA FILE=WPIDS ABB=ON  PLU=ON  QUILLAJA OR (QS OR QA)(W) 21 OR
                 QA 21V1
L58         2162 SEA FILE=WPIDS ABB=ON  PLU=ON  SAPONIN
L59        13939 SEA FILE=WPIDS ABB=ON  PLU=ON  ?STEROL
L60        19469 SEA FILE=WPIDS ABB=ON  PLU=ON  ?LIPID
L61        19835 SEA FILE=WPIDS ABB=ON  PLU=ON  VACCIN?
L62        92215 SEA FILE=WPIDS ABB=ON  PLU=ON  IMMUN?
L63           34 SEA FILE=WPIDS ABB=ON  PLU=ON  L57 AND (L59 OR L60) AND (L61
                 OR L62)
L65           88 SEA FILE=WPIDS ABB=ON  PLU=ON  L58 AND (L59 OR L60) AND (L61
                 OR L62) NOT L63
L66           12 SEA FILE=WPIDS ABB=ON  PLU=ON  L65 AND SAPONIN/TI AND (CHOLESTE
                 ROL OR STEROL OR EMULSION?)/TI


L57          128 SEA FILE=WPIDS ABB=ON  PLU=ON  QUILLAJA OR (QS OR QA)(W) 21 OR
                 QA 21V1
L58         2162 SEA FILE=WPIDS ABB=ON  PLU=ON  SAPONIN
L59        13939 SEA FILE=WPIDS ABB=ON  PLU=ON  ?STEROL
L60        19469 SEA FILE=WPIDS ABB=ON  PLU=ON  ?LIPID
L61        19835 SEA FILE=WPIDS ABB=ON  PLU=ON  VACCIN?
L62        92215 SEA FILE=WPIDS ABB=ON  PLU=ON  IMMUN?
L63           34 SEA FILE=WPIDS ABB=ON  PLU=ON  L57 AND (L59 OR L60) AND (L61
                 OR L62)
L65           88 SEA FILE=WPIDS ABB=ON  PLU=ON  L58 AND (L59 OR L60) AND (L61
                 OR L62) NOT L63
L67            2 SEA FILE=WPIDS ABB=ON  PLU=ON  L65 AND ((QUIL/TI AND STEROL/TI)
                  OR (AMPIPHILIC OR AGGREGATES)/TI)


=> s l64 or l66 or l67
L71           24 L64 OR L66 OR L67

=> dup rem l24 l68 l71 l69 l70
FILE 'MEDLINE' ENTERED AT 15:53:20 ON 17 FEB 2004

FILE 'CAPLUS' ENTERED AT 15:53:20 ON 17 FEB 2004
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PROCESSING COMPLETED FOR L24
PROCESSING COMPLETED FOR L68
PROCESSING COMPLETED FOR L71
PROCESSING COMPLETED FOR L69
PROCESSING COMPLETED FOR L70
L72           64 DUP REM L24 L68 L71 L69 L70 (13 DUPLICATES REMOVED)
                 ANSWERS '1-4' FROM FILE MEDLINE
                 ANSWERS '5-21' FROM FILE CAPLUS
                 ANSWERS '22-34' FROM FILE WPIDS
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ANSWERS '35-57' FROM FILE EMBASE
ANSWERS '58-64' FROM FILE BIOSIS

=> d ibib ab l72 1-64

L72 ANSWER 1 OF 64 MEDLINE on STN
ACCESSION NUMBER: 2002694661 MEDLINE
DOCUMENT NUMBER: 22343847 PubMed ID: 12455400
TITLE: Novel adjuvant systems.
AUTHOR: McCluskie M J; Weeratna R D
CORPORATE SOURCE: Coley Pharmaceutical Canada, 725 Parkdale Avenue, Ottawa, K1Y 4E9, Canada.. mmccluskie@coleypharma.com
SOURCE: Curr Drug Targets Infect Disord, (2001 Nov) 1 (3) 263-71. Ref: 138
Journal code: 101128002. ISSN: 1568-0053.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021214
Last Updated on STN: 20021217
Entered Medline: 20021212

AB Vaccination remains the single most valuable tool in the prevention of infectious disease. Nevertheless, there exists a need to improve the performance of existing vaccines such that fewer boosts are needed or to develop novel vaccines. For the development of effective vaccines for humans, a great need exists for safe and effective adjuvants. A number of novel adjuvants have been reported in recent years including: i) bacterial toxins such as cholera toxin, CT, and the Escherichia coli heat-labile enterotoxin, LT; ii) less toxic derivatives of CT and LT; iii) endogenous human immunomodulators, such as IL-2, IL-12, GM-CSF; iv) hormones; v) lipopeptides; vi) saponins, such as QS-21; vii) synthetic oligonucleotides containing CpG motifs (CpG ODN); viii) lipid 'A derivatives, such as monophosphoryl lipid A, MPL, and ix) muramyl dipeptide (MDP) derivatives. Herein, we will review recent findings using these novel adjuvant systems.

L72 ANSWER 2 OF 64 MEDLINE on STN
ACCESSION NUMBER: 2000165438 MEDLINE
DOCUMENT NUMBER: 20165438 PubMed ID: 10699704
TITLE: Hydration of lipid films with an aqueous solution of Quil A: a simple method for the preparation of immune-stimulating complexes.
AUTHOR: Copland M J; Rades T; Davies N M
CORPORATE SOURCE: School of Pharmacy, University of Otago, Formulation and Drug Delivery Group, PO Box 913, Dunedin, New Zealand.
SOURCE: INTERNATIONAL JOURNAL OF PHARMACEUTICS, (2000 Mar 10) 196 (2) 135-9.
Journal code: 7804127. ISSN: 0378-5173.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000511

AB Immune-stimulating complexes (ISCOMs) are stable colloidal complexes of

the adjuvant Quil A, cholesterol and phospholipid, which are effective carriers for subunit vaccines. The techniques currently available for the preparation of ISCOMs from the constituent components are rather complex and are based on either centrifugation or dialysis. This note reports a new simple procedure for the preparation of ISCOM matrices based on hydration of a cholesterol/phospholipid film with an aqueous solution of Quil A. It is demonstrated that ISCOM matrices do not form in the absence of phospholipid when prepared by this method. Further, the ratio by weight of phospholipid to either cholesterol or Quil A must be greater than that required for preparation by either dialysis or centrifugation. Photon correlation spectroscopy, negative stain transmission electron microscopy and centrifugation through a sucrose gradient demonstrate that ISCOM matrices can be prepared from cholesterol/lipid films by hydration with an aqueous solution of Quil A when the ratio of phospholipid:cholesterol:Quil A by weight is 6:1:4, respectively. Lower ratios of phospholipid:cholesterol reduce the efficiency of ISCOM formation while higher ratios produce systems containing a mixture of ISCOMs together with liposomes.

L72 ANSWER 3 OF 64 MEDLINE on STN
ACCESSION NUMBER: 1998350542 MEDLINE
DOCUMENT NUMBER: 98350542 PubMed ID: 9685925
TITLE: Biodegradable implants for the delivery of veterinary vaccines: design, manufacture and antibody responses in sheep.
AUTHOR: Walduck A K; Opdebeeck J P; Benson H E; Prankerd R
CORPORATE SOURCE: Department of Parasitology, University of Queensland, Australia.. annaw@qimr.edu.au
SOURCE: JOURNAL OF CONTROLLED RELEASE, (1998 Feb 12) 51 (2-3) 269-80.
Journal code: 8607908. ISSN: 0168-3659.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19981006
Last Updated on STN: 19981006
Entered Medline: 19980921

AB Biodegradable implants made from cholesterol and lecithin (C:L) were used to deliver a recombinant antigen (recombinant Dichelobacter nodosus pili) and adjuvant (Quil A) to sheep. Implants (5.5- x 1.8-mm) were placed subcutaneously and compared to a conventional vaccination regime (2 injections, 4 weeks apart) for antibody responses and tissue compatibility. Release profiles of antigen and adjuvant were also studied in vitro and in vivo. The presence of Quil A in vaccine implants had a marked effect on the rate at which antigen was released with 29 and 44% being released in the first 24 h from implants containing pili alone and pili with Quil A, respectively. Sheep produced significant levels of antibody when immunized with implants, however the response was short-lived and of significantly lower intensity than the response stimulated by two injections of antigen with Quil A ($P < 0.01$). A second implant system was developed where implants coated with C:L to delay antigen release, were used in combination with uncoated implants to deliver a priming dose and boosting dose of antigen. Antibody titres stimulated by the 4 double implant system were equivalent to those stimulated by a conventional regime of two injections (four weeks apart) for the first six weeks of the experiment. After this time, antibody levels in the groups which received implants dropped significantly. In vitro studies revealed that some of the implant coatings had caused a

delay in the release of antigen (the rate of release peaked at 72 h), however this was not long enough to provide a significant boosting effect. In all cases, implants were well tolerated by sheep and caused less local reaction than injected vaccines.

L72 ANSWER 4 OF 64 MEDLINE on STN
ACCESSION NUMBER: 1998074568 MEDLINE
DOCUMENT NUMBER: 98074568 PubMed ID: 9413088
TITLE: Effects of carbohydrate modification of Quillaja saponaria Molina QH-B fraction on adjuvant activity, cholesterol-binding capacity and toxicity.
AUTHOR: Ronnberg B; Fekadu M; Behboudi S; Kenne L; Morein B
CORPORATE SOURCE: Department of Iscom Technology, National Veterinary Institute, Uppsala, Sweden.
SOURCE: VACCINE, (1997 Dec) 15 (17-18) 1820-6.
Journal code: 8406899. ISSN: 0264-410X.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980306
Last Updated on STN: 19980306
Entered Medline: 19980223

AB The iscom is an efficient antigen-presenting system for various antigens inducing both MHC class I and class II restricted immune responses. Protective immunity has been evoked against a variety of infectious agents. The saponin adjuvant Quil A, which was originally used to form iscoms, is composed of a mixture of structurally similar triterpenoids from Quillaja saponaria Molina having different biological activities. A purified, toxic Quillaja triterpenoid fraction with strong adjuvant activity, designated QH-B, was used to study whether modification of the carbohydrate moiety with sodium periodate would alter the toxicity without harming adjuvant activity and cholesterol-binding capacity. Most sugars, and in particular Api, Gal and Xyl, were modified by periodate treatment with only minor changes of the molecular weights indicating no loss of sugar residues. The adjuvant activity of QH-B was reduced in a dose-related manner, and at a concentration of 25 mM sodium periodate a significant reduction in toxicity was observed. The differences in both toxicity and adjuvant activity of the periodate-treated QH-B could be derived from alterations in the structure of the sugars Gal and Xyl, while modification of Api may influence adjuvant activity but not toxicity in vivo. The cholesterol-binding capacity, a prerequisite for iscom formation, was not affected by periodate oxidation at the doses tested. However, the use of modified QH-B as described in the present study for iscom-matrix formation resulted in "saponin-lipid complexes" which, to a various degree or totally, deviated from the characteristic iscom morphology.

L72 ANSWER 5 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2003:282425 CAPLUS
DOCUMENT NUMBER: 138:302637
TITLE: Intradermal vaccine compositions comprising saponin, sterol, and LPS derivative or CpG oligonucleotide as adjuvant
INVENTOR(S): Garcon, Nathalie
PATENT ASSIGNEE(S): Glaxosmithkline Biologicals S.A., Belg.
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003028760	A2	20030410	WO 2002-EP10931	20020930

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2001-23580 A 20011001

AB The present invention provides novel intradermal **vaccines** and novel uses for adjuvants in the preparation of intradermal **vaccines**, and also novel methods of treatment comprising them. The intradermal adjuvants, and methods, of the present invention comprise a saponin and a sterol, wherein the saponin and sterol are formulated in a liposome. The intradermal vaccine further comprises a LPS derivative or an immunostimulatory CpG oligonucleotide. The intradermal adjuvants are used in the manufacture of intradermal **vaccines** for humans, and in the intradermal treatment of humans.

L72 ANSWER 6 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2000:116922 CAPLUS
DOCUMENT NUMBER: 132:171114
TITLE: Vaccine ISCOM adjuvant using saponin as sole detergent
INVENTOR(S): Friede, Martin; Garcon, Nathalie
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals SA, Belg.
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000007621	A2	20000217	WO 1999-EP5587	19990803
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2339486	AA	20000217	CA 1999-2339486	19990803
AU 9955099	A1	20000228	AU 1999-55099	19990803
AU 738965	B2	20011004		
EP 1102600	A2	20010530	EP 1999-941506	19990803
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002522397	T2	20020723	JP 2000-563304	19990803
US 6506386	B1	20030114	US 2001-744800	20010604

PRIORITY APPLN. INFO.: GB 1998-17052 A 19980805
WO 1999-EP5587 W 19990803

AB The present invention provides an improved adjuvant formulation and a process for producing said adjuvant. The adjuvant comprises an ISCOM

structure comprising a saponin, said ISCOM structure being devoid of addnl. detergent.

L72 ANSWER 7 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1999:7859 CAPLUS
DOCUMENT NUMBER: 130:65237
TITLE: Ganglioside immunostimulating complexes and uses thereof
INVENTOR(S): Cox, John Cooper; Ronnberg, Bengt John Lennart; Sjolander, Sigrid Elisabet
PATENT ASSIGNEE(S): Eriksson, Lennart, Australia; CSL Limited
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856420	A1	19981217	WO 1998-AU453	19980612
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9880035	A1	19981230	AU 1998-80035	19980612
AU 725342	B2	20001012		
ZA 9805140	A	19990107	ZA 1998-5140	19980612
EP 1019087	A1	20000719	EP 1998-928010	19980612
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 501641	A	20001222	NZ 1998-501641	19980612
JP 2002504101	T2	20020205	JP 1999-501150	19980612

PRIORITY APPLN. INFO.: AU 1997-7329 A 19970612
WO 1998-AU453 W 19980612

AB The present invention relates generally to an immunostimulating complex comprising one or more gangliosides and more particularly to an immunostimulating complex comprising at least one of the gangliosides GM2, GD2, GD3 or GT3. The immunogenic immunostimulating complex also comprises a saponin preparation, a sterol, a protein epitope, and phospholipid. The protein may be cancer specific protein, melanoma specific protein, or influenza hemagglutinin. The present invention is useful, inter alia, as a prophylactic and/or therapeutic agent in the treatment of tumors, and more particularly, melanomas.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L72 ANSWER 8 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1998:721602 CAPLUS
DOCUMENT NUMBER: 129:342686
TITLE: Anti-Helicobacter vaccine composition comprising a Th1 adjuvant
INVENTOR(S): Guy, Bruno; Haensler, Jean
PATENT ASSIGNEE(S): Merieux Oravax, Fr.
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9848836	A1	19981105	WO 1998-FR875	19980430
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2762787	A1	19981106	FR 1997-5608	19970430
FR 2762787	B1	20001006		
AU 9876584	A1	19981124	AU 1998-76584	19980430
AU 750379	B2	20020718		
EP 979100	A1	20000216	EP 1998-924360	19980430
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9809381	A	20000704	BR 1998-9381	19980430
JP 2002505665	T2	20020219	JP 1998-546684	19980430

PRIORITY APPLN. INFO.: FR 1997-5608 A 19970430
FR 1997-15732 A 19971208
WO 1998-FR875 W 19980430

OTHER SOURCE(S): MARPAT 129:342686

AB The invention concerns the use of an immunogenic agent derived from Helicobacter, associated with an adjuvant such as QS-21, DC-chol or Bay R1005, for making a pharmaceutical composition designed to induce an immune response of the T helper 1 type (Th1), for preventing or treating Helicobacter infection in a mammal.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L72 ANSWER 9 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 1998:604833 CAPLUS
DOCUMENT NUMBER: 129:215712
TITLE: Chelating immunostimulating complexes
INVENTOR(S): MacFarlan, Roderick Ian; Malliaros, Jim
PATENT ASSIGNEE(S): Csl Ltd., Australia
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9836772	A1	19980827	WO 1998-AU80	19980213
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				

AU 9858488	A1	19980909	AU 1998-58488	19980213
AU 720855	B2	20000615		
NZ 336792	A	20000128	NZ 1998-336792	19980213
EP 986399	A1	20000322	EP 1998-901888	19980213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001512464	T2	20010821	JP 1998-536076	19980213
ZA 9801281	A	19981119	ZA 1998-1281	19980217
US 2002081329	A1	20020627	US 1999-367309	19990811
US 6428807	B2	20020806		

PRIORITY APPLN. INFO.: AU 1997-5178 A 19970219
WO 1998-AU80 W 19980213

AB An immunostimulating complex matrix comprising a saponin preparation, a sterol and a phospholipid, the matrix further comprising a metal-chelating moiety capable of binding a protein or polypeptide having at least one chelating amino acid sequence in the presence of metal ions. An immunogenic immunostimulating complex which comprises this matrix and an immunogenic protein or polypeptide having at least one chelating amino acid sequence, the protein or polypeptide being bound to the matrix in the presence of metal ions. ISCOM comprising ISCOPREP703 (a Quillaja saponin mixture), cholesterol, and DPPC was prepared and used as adjuvant for vaccine containing fusion protein of HPV-16 E6 and E7 and hexahistidine sequence, and for vaccine containing recombinant family C protein of Helicobacter pylori with hexahistidine sequence.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L72 ANSWER 10 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1998:239123 CAPLUS
DOCUMENT NUMBER: 128:307514
TITLE: **Vaccines** for infections and cancers
INVENTOR(S): Garcon, Nathalie; Friede, Martin
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals SA, Belg.; Garcon, Nathalie; Friede, Martin
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9815287	A1	19980416	WO 1997-EP5578	19970930
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9747812	A1	19980505	AU 1997-47812	19970930
AU 714930	B2	20000113		
BR 9711853	A	19990824	BR 1997-11853	19970930
EP 939650	A1	19990908	EP 1997-910430	19970930
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
CN 1238696	A	19991215	CN 1997-180166	19970930
NZ 334734	A	20000526	NZ 1997-334734	19970930

JP 2001501640	T2	20010206	JP 1998-517196		19970930
ZA 9708868	A	19990406	ZA 1997-8868		19971003
NO 9901524	A	19990329	NO 1999-1524		19990329
KR 2000048866	A	20000725	KR 1999-702874		19990402
US 2001053365	A1	20011220	US 2001-819464		20010328
PRIORITY APPLN. INFO.:			GB 1996-20795	A	19961005
			GB 1995-8326	A	19950425
			EP 1996-910019	A	19960401
			WO 1996-EP1464	W	19960401
			WO 1997-EP5578	W	19970930
			US 1997-945450	B2	19971212
			US 1999-269383	W	19990402

AB The invention relates to a vaccine composition comprising an antigen and an adjuvant composition for treating infections or cancer. The adjuvant composition comprises alum, an immunol. active saponin fraction (e.g. QS21) associated with liposome containing a phospholipid and a sterol (e.g. cholesterol), and 3-de-O-acylated monophosphoryl lipid A. The antigen is derived from human immunodeficiency virus, feline immunodeficiency virus, varicella zoster virus, herpes simplex virus type 1 and 2, human cytomegalovirus, hepatitis A, B, C or E, respiratory syncytial virus, human papilloma virus, influenza virus, Hib, meningitis virus, Salmonella, Neisseria, Borrelia, Chlamydia, Bordetella, Plasmodium, Toxoplasma, or cancer.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L72 ANSWER 11 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1996:761906 CAPLUS
DOCUMENT NUMBER: 126:37039
TITLE: **Vaccines** containing a saponin and a sterol
INVENTOR(S): Garcon, Nathalie Marie-Josephe Claude; Friede, Martin
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals SA, Belg.; Garcon, Nathalie Marie-Josephe Claude; Friede, Martin
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9633739	A1	19961031	WO 1996-EP1464	19960401
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
CA 2217178	AA	19961031	CA 1996-2217178	19960401
AU 9653345	A1	19961118	AU 1996-53345	19960401
AU 693022	B2	19980618		
EP 822831	A1	19980211	EP 1996-910019	19960401
EP 822831	B1	19991124		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
CN 1182370	A	19980520	CN 1996-193443	19960401
CN 1111071	B	20030611		
EP 884056	A1	19981216	EP 1998-201600	19960401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				

JP 11504020	T2	19990406	JP 1996-532122	19960401
BR 9608199	A	19990518	BR 1996-8199	19960401
EP 955059	A2	19991110	EP 1999-201323	19960401
EP 955059	A3	20000712		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
AT 186842	E	19991215	AT 1996-910019	19960401
ES 2140076	T3	20000216	ES 1996-910019	19960401
SK 282017	B6	20011008	SK 1997-1442	19960401
PL 184061	B1	20020830	PL 1996-322968	19960401
ZA 9602612	A	19960829	ZA 1996-2612	19960402
IL 118004	A1	19991130	IL 1996-118004	19960423
TW 515715	B	20030101	TW 1996-85104841	19960423
NO 9704859	A	19971021	NO 1997-4859	19971021
BG 63491	B1	20020329	BG 1997-101995	19971024
AU 9869873	A1	19980723	AU 1998-69873	19980603
AU 699213	B2	19981126		
US 2001053365	A1	20011220	US 2001-819464	20010328

PRIORITY APPLN. INFO.:

GB 1995-8326	A	19950425
GB 1995-13107	A	19950628
EP 1996-910019	A3	19960401
WO 1996-EP1464	W	19960401
GB 1996-20795	A	19961005
WO 1997-EP5578	W	19970930
US 1997-945450	B2	19971212
US 1999-269383	W	19990402

AB A vaccine composition comprises an antigen, an immunol. active saponin fraction and a sterol. An example saponin is QS21 and example sterol is cholesterol.

L72 ANSWER 12 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1996:410535 CAPLUS
DOCUMENT NUMBER: 125:56216
TITLE: Saponin preparations and use thereof in ISCOMs
INVENTOR(S): Cox, John Cooper; Coulter, Alan Robert; Morein, Bror; Lovgren-Bengtsson, Karin; Sundquist, Bo
PATENT ASSIGNEE(S): Iscotec Ab, Swed.
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9611711	A1	19960425	WO 1995-AU670	19951012
W: AU, CA, FI, JP, KR, NO, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2201611	AA	19960425	CA 1995-2201611	19951012
AU 9536444	A1	19960506	AU 1995-36444	19951012
AU 686891	B2	19980212		
ZA 9508600	A	19970414	ZA 1995-8600	19951012
EP 785802	A1	19970730	EP 1995-933981	19951012
EP 785802	B1	20011212		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10508301	T2	19980818	JP 1995-512788	19951012
NZ 333608	A	20010330	NZ 1995-333608	19951012
AT 210463	E	20011215	AT 1995-933981	19951012
NO 9701622	A	19970610	NO 1997-1622	19970409

FI 9701498	A	19970610	FI 1997-1498		19970410
US 6352697	B1	20020305	US 1999-809987		19990222
PRIORITY APPLN. INFO.:			AU 1994-8732	A	19941012
			NZ 1995-293882	A1	19951012
			WO 1995-AU670	W	19951012

AB A preparation of saponins of Quillaja saponaria, comprises fractions of Quil A having good adjuvant activity, low hemolytic activity and good ability to form immunostimulatory complexes (ISCOMs). Quil A fractions (QH-A.apprx.C and QH703) were purified from Quillaja bark extract, formed ISCOMs with cholesterol and/or phosphatidylcholine, and used as vaccine adjuvant for influenza virus HA or diphtheria toxoid. Interleukin 1 induction by various mixts. of Quillaja saponins induces, and clin. safety of ISCOM matrix prepared from QH703 in human were also demonstrated.

L72 ANSWER 13 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 10
ACCESSION NUMBER: 1992:446550 CAPLUS
DOCUMENT NUMBER: 117:46550
TITLE: Immunogenic complexes, in particular iscoms, containing Quil A fractions
INVENTOR(S): Kersten, Gideon Frank Anne; Spiekstra, Arjen; Van de Werken, Gerrit; Beuvery, Eduard Coen
PATENT ASSIGNEE(S): De Staat der Nederlanden Vertegenwoordigd Door de Minister Van Welzijn Volksgezondheid en Cultuur, Neth.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9206710	A1	19920430	WO 1991-NL211	19911023
W: CA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
NL 9002314	A	19920518	NL 1990-2314	19901023
CA 2094600	AA	19920424	CA 1991-2094600	19911023
CA 2094600	C	19981208		
EP 555276	A1	19930818	EP 1991-918619	19911023
EP 555276	B1	19950830		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ES 2075964	T3	19951016	ES 1991-918619	19911023
US 5620690	A	19970415	US 1993-39294	19930419
PRIORITY APPLN. INFO.:			NL 1990-2314 A	19901023
			WO 1991-NL211 W	19911023

AB Immunogenic complexes, especially iscoms, are composed of sterol(s), saponin(s), and, in the case of iscoms, a phospholipid, characterized in that the saponin is ≥1 fraction derived from Quil A by means of hydrophobic interaction chromatog. and have the designations QA 1 to QA 23. The complex may also have antigenic protein(s) or peptide(s) for **vaccines**. Quil A fractions were separated on a Supelcosil LC-18 semiprep. column and characterized. All fractions possessed an adjuvant activity; however, PIC3 protein (pore protein I from Neisseria gonorrhoea strain C3) iscoms containing Quil A fraction QA 3 showed outstanding results in mice. The structure of QA 3 was further characterized.

L72 ANSWER 14 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 12
ACCESSION NUMBER: 1991:115082 CAPLUS
DOCUMENT NUMBER: 114:115082
TITLE: Sterol-containing iscom matrix with immunostimulating

activity

INVENTOR(S): Morein, Bror; Loevgren, Karin; Dalsgaard, Kristian; Thurin, Jan; Sundquist, Bo

PATENT ASSIGNEE(S): Swed.

SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9003184	A1	19900405	WO 1989-SE528	19890928
W: AU, DK, FI, HU, JP, NO, SU, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
ZA 8907217	A	19900627	ZA 1989-7217	19890921
ES 2029758	A6	19920901	ES 1989-3266	19890927
CA 1338888	A1	19970204	CA 1989-613745	19890927
AU 8943374	A1	19900418	AU 1989-43374	19890928
AU 632067	B2	19921217		
EP 436620	A1	19910717	EP 1989-911115	19890928
EP 436620	B1	19940810		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
HU 56722	A2	19911028	HU 1989-5758	19890928
JP 04501714	T2	19920326	JP 1989-510329	19890928
JP 2501650	B2	19960529		
RU 2120302	C1	19981020	RU 1989-4895211	19890928
NO 9101049	A	19910503	NO 1991-1049	19910315
DK 9100558	A	19910529	DK 1991-558	19910327
US 5679354	A	19971021	US 1991-671816	19910521

PRIORITY APPLN. INFO.:

US 1988-251576	19880930
SE 1989-1027	19890322
SE 1989-2780	19890816
WO 1989-SE528	19890928

AB An iscom matrix, which is not a lipid vesicle, comprises >1 sterol and >1 saponin, but no intentional antigenic determinants, and optionally also adjuvants. The matrix is an immunostimulant, usable in medicines, **vaccines**, kits, etc. At least one sterol is solubilized in a solvent or detergent, the saponin or saponins are added, the other adjuvants and lipids are optionally added. The organic solvent or the detergent may be removed for example by dialysis, ultrafiltration, gel filtration or electrophoresis. The sterol and saponin might also be solubilized in the lipids and/or adjuvants. A solution of 1 mg cholesterol and 5 mg Quil A in aqueous 20% MEGA-10 was dialyzed against PBS, followed by pelleting through 30% sucrose and dissoln. of the pelleted matrixes in PBS, at 1 mg/mL. The matrix (0.1 μg) enhanced the immune response to influenza virus envelope protein, in mice. Extraction of Quil A from Quillaja saponaria bark, is described. Three components (B2, B3 and B4B) are separated and characterized.

L72 ANSWER 15 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 13

ACCESSION NUMBER: 1987:605167 CAPLUS

DOCUMENT NUMBER: 107:205167

TITLE: Process for preparing immunological complexes and pharmaceutical composition containing these complexes

INVENTOR(S): De Vries, Petra; Van Wezel, Antonius Ludovicus; Beuvery, Eduard Coen

PATENT ASSIGNEE(S): De Staat der Nederlanden Vertegenwoordigd Door de Minister van Welzijn, Volksgezondheid en Cultuur,

Neth.
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 231039	A1	19870805	EP 1987-200035	19870113
EP 231039	B1	19920108		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
DK 8700150	A	19870715	DK 1987-150	19870113
DK 166762	B1	19930712		
AT 71303	E	19920115	AT 1987-200035	19870113
ES 2039229	T3	19930916	ES 1987-200035	19870113
JP 63002933	A2	19880107	JP 1987-7384	19870114
JP 2502558	B2	19960529		
US 4900549	A	19900213	US 1987-3070	19870114
CA 1279012	A1	19910115	CA 1987-527289	19870114
JP 08208513	A2	19960813	JP 1995-309056	19951128
JP 2703528	B2	19980126		

PRIORITY APPLN. INFO.: NL 1986-66 19860114
EP 1987-200035 19870113

AB An immunogenic complex is prepared by contacting an amphoteric antigenic protein or peptide in dissolved or solubilized form with a solution containing a detergent, a sterol, and a glycoside comprising hydrophobic and hydrophobic regions in at least the critical micelle forming concentration with subsequent removal of the detergent and purification of the formed immunogenic complex. Measles virus fusion protein was produced and purified by known methods and incorporated into an immunogenic complex by treating fusion protein (60 μg) with 180 μL Tris-HCl (pH 7.8), 150 mM NaCl, 2% octylglucoside, and 350 μg phosphatidylethanolamine and 350 μg cholesterol in 700 μL 2% octylglucoside for 1 h at room temperature, addition of 1.7 mg Quil A (10% weight/volume), removal of octylglucoside by dialysis against 10 mM Tris-HCl (pH 7.8) and 150 mM NaCl for 16 h at 4°, and purification via ultracentrifugation (continuous sucrose gradient), and electron microscope examination of the product-containing fractions (micrograph shown).

L72 ANSWER 16 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:183750 CAPLUS
DOCUMENT NUMBER: 136:226816
TITLE: The diagnosis, prevention, and/or successful treatment of atherosclerosis, infectious diseases, and disturbances in the immune system
INVENTOR(S): Cabezas, Manuel Castro; Van Dijk, Hans
PATENT ASSIGNEE(S): Universitair Medisch Centrum Utrecht, Neth.
SOURCE: Eur. Pat. Appl., 26 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1186299	A1	20020313	EP 2000-203156	20000912
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO
WO 2002022160 A2 20020321 WO 2001-NL672 20010912
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
WO 2002022161 A2 20020321 WO 2001-NL673 20010912
WO 2002022161 A3 20020808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2001094401 A5 20020326 AU 2001-94401 20010912
AU 2001094402 A5 20020326 AU 2001-94402 20010912
EP 1318831 A2 20030618 EP 2001-975032 20010912
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
EP 1318832 A2 20030618 EP 2001-975033 20010912
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
US 2003143223 A1 20030731 US 2002-327604 20021220
US 2003165458 A1 20030904 US 2002-327631 20021220
PRIORITY APPLN. INFO.: EP 2000-203156 A 20000912
US 2000-253465P P 20001128
WO 2001-NL672 W 20010912
WO 2001-NL673 W 20010912

AB Complement is recognized as an important, humoral defense system involved in the innate (nonspecific) recognition and elimination of microbial invaders, other foreign particles or mols., and antigen-antibody complexes from the body. The present invention makes use of the surprising notion that the handling of lipids by the body, rather than its antimicrobial activity, is the primary and most ancient function of the complement system. Consequently, atherosclerosis as observed in disorders associated with disturbed lipid metabolism (familial combined hyperlipemia [FCHL], postprandial hyperlipidemia, hypertriglyceridemia with low levels of HDL cholesterol, and insulin resistance associated with type-II diabetes and obesity), must be ascribed to either genetic or acquired defects in ancient (activatory and/or regulatory) complement components. Based on this new insight, novel preventive measures and treatment modalities of disturbed lipid metabolism are introduced. Other implications of the same invention, based on the notion that lipoproteins and lymphocytes share the lymph pathway to arrive in the blood circulation, are that the lipid metabolizing system may be employed to effectively manipulate the immune system. Based on this aspect of the invention, novel oral vaccination and oral immunomodulation strategies are introduced as well.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L72 ANSWER 17 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:50511 CAPLUS

DOCUMENT NUMBER: 134:114821
TITLE: Recombinant envelope vaccine against Flavivirus infection
INVENTOR(S): Ivy, John; Bignami, Gary; Mcdonell, Michael; Clements, David E.; Coller, Beth-Ann G.
PATENT ASSIGNEE(S): Hawaii Biotechnology Group, Inc., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001003729	A2	20010118	WO 2000-US18876	20000712
WO 2001003729	A3	20020912		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6432411	B1	20020813	US 1999-352387	19990713
BR 2000013154	A	20020604	BR 2000-13154	20000712

PRIORITY APPLN. INFO.: US 1999-352387 A 19990713
WO 2000-US18876 W 20000712

AB A vaccine contains at least one Drosophila cell-secreted, recombinantly-produced form of a truncated Flavivirus envelope glycoprotein, as an active ingredient, and an adjuvant, as a critical component of the vaccine. The adjuvant is an immunomodulating agent having an iscom-like structure and comprising within the iscom-like structure at least one lipid and at least one saponin, and a pharmaceutically acceptable vehicle. Such a vaccine protects a subject against infection by a Flavivirus.

L72 ANSWER 18 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:240985 CAPLUS
DOCUMENT NUMBER: 132:292701
TITLE: Novel methods for therapeutic vaccination
INVENTOR(S): Steinaa, Lucilla; Mouritsen, Soren; Nielsen, Klaus Gregorious; Haaning, Jesper; Leach, Dana; Dalum, Iben; Gautam, Anand; Birk, Peter; Karlsson, Gunilla
PATENT ASSIGNEE(S): M & E Biotech A/S, Den.
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020027	A2	20000413	WO 1999-DK525	19991005
WO 2000020027	A3	20001012		
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, EE, EE, ES, FI, FI, GB, GD, GE,				

GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO,
RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2345817	AA	20000413	CA 1999-2345817	19991005
AU 9958510	A1	20000426	AU 1999-58510	19991005
AU 751709	B2	20020822		
EP 1117421	A2	20010725	EP 1999-945967	19991005
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, IE, SI, LT, LV, FI, RO				
JP 2002526419	T2	20020820	JP 2000-573386	19991005
EE 200100203	A	20021015	EE 2001-203	19991005
NZ 511055	A	20031031	NZ 1999-511055	19991005
NO 2001001586	A	20010531	NO 2001-1586	20010328
ZA 2001002603	A	20020930	ZA 2001-2603	20010329
HR 2001000319	A1	20020630	HR 2001-319	20010504

PRIORITY APPLN. INFO.:

DK 1998-1261	A	19981005
US 1998-105011P	P	19981020
WO 1999-DK525	W	19991005

AB A method is disclosed for inducing cell-mediated immunity against cellular antigens. More specifically, the invention provides for a method for inducing cytotoxic T-lymphocyte immunity against weak antigens, notably self-proteins. The method entails that antigen presenting cells are induced to present at least one CTL epitope of the weak antigen and at the same time presenting at least one foreign T-helper lymphocyte epitope. In a preferred embodiment, the antigen is a cancer specific antigen, e.g. prostate specific membrane antigen (PSM), Her2, or FGF8b. The method can be exercised by using traditional polypeptide vaccination, but also by using live attenuated vaccines or nucleic acid vaccination. The invention furthermore provides immunogenic analogs of PSM, Her2 and FGF8b, as well as nucleic acid mols. encoding these analogs. Also vectors and transformed cells are disclosed. The invention also provides for a method for identification of immunogenic analogs of weak or non-immunogenic antigens.

L72 ANSWER 19 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:133557 CAPLUS
DOCUMENT NUMBER: 132:193246
TITLE: Compositions of CpG and saponin adjuvants and methods thereof
INVENTOR(S): Kensil, Charlotte A.
PATENT ASSIGNEE(S): Aquila Biopharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000009159	A1	20000224	WO 1999-US17956	19990806

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG,

KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2340174	AA	20000224	CA 1999-2340174	19990806
AU 9953953	A1	20000306	AU 1999-53953	19990806
EP 1104306	A1	20010606	EP 1999-939711	19990806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001034330	A1	20011025	US 2001-760506	20010112

PRIORITY APPLN. INFO.:

US 1998-95913P	P	19980810
US 1999-128608P	P	19990408
WO 1999-US17956	W	19990806
US 2000-175840P	P	20000113
US 2000-200853P	P	20000501

OTHER SOURCE(S): MARPAT 132:193246

AB Disclosed are vaccine compns. comprising immunostimulatory oligonucleotides and saponin adjuvants and antigens and the use thereof for stimulating immunity, enhancing cell-mediated immunity, and enhancing antibody production Also described are immune adjuvant compns. comprising immunostimulatory oligonucleotides and saponin adjuvants, as well as methods for increasing an immune response using the same.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L72 ANSWER 20 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:822526 CAPLUS
DOCUMENT NUMBER: 134:9337
TITLE: Adjuvant optimized for stability and biocompatibility for enhancing humoral and cellular immune responses
INVENTOR(S): Mueller, Rainer Helmut; Grubhofer, Nikolaus; Olbrich, Carsten
PATENT ASSIGNEE(S): Gerbu G.m.b.H., Germany; Pharmasol G.m.b.H.
SOURCE: Ger. Offen., 26 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 10024788	A1	20001123	DE 2000-10024788	20000519
WO 2000071154	A2	20001130	WO 2000-EP4565	20000519
WO 2000071154	A3	20010628		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
BR 2000010823	A	20020305	BR 2000-10823	20000519
EP 1183045	A2	20020306	EP 2000-936761	20000519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003500365	T2	20030107	JP 2000-619456	20000519
WO 2000071077	A2	20001130	WO 2000-EP4644	20000522

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 2000058091	A5	20001212	AU 2000-58091	20000522
ZA 2001009147	A	20020508	ZA 2001-9147	20011106

PRIORITY APPLN. INFO.:

DE 1999-19923256	A1	19990520
WO 2000-EP4565	W	20000519
WO 2000-EP4644	W	20000522

AB A title adjuvant is disclosed for injection in combination with an antigen. The adjuvant consists of solid lipid particles or solid lipid mixts. It can be used for manufacture of efficient and biocompatible **vaccines** for immunization of human and other animals as well as for the production of antibodies. By selection of the particle size, particle charge, and particle surface properties the strength of the immune response can be modulated. The optimized adjuvant can be used in combination with other adjuvants such as mol. adjuvants like GMDP.

L72 ANSWER 21 OF 64 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:194018 CAPLUS
DOCUMENT NUMBER: 130:227707
TITLE: Vaccine adjuvant emulsions containing oils, saponins, and sterols and immunomodulators
INVENTOR(S): Garcon, Nathalie; Momin, Patricia Marie Christine Aline Francoise
PATENT ASSIGNEE(S): Smithkline Beecham Biologicals SA, Belg.
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9912565	A1	19990318	WO 1998-EP5714	19980902

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2302637	AA	19990318	CA 1998-2302637	19980902
AU 9896238	A1	19990329	AU 1998-96238	19980902
EP 1009430	A1	20000621	EP 1998-950005	19980902

R: BE, CH, DE, ES, FR, GB, IT, LI, NL

JP 2001515870	T2	20010925	JP 2000-510462	19980902
US 6372227	B1	20020416	US 2000-486996	20000424
US 2002058047	A1	20020516		

PRIORITY APPLN. INFO.:

GB 1997-18901	A	19970905
WO 1998-EP5714	W	19980902

AB The present invention relates to an oil-in-water emulsion compns., their use in medicine, in particular to their use in augmenting immune responses

to a wide range of antigens, and to methods of their manufacture The emulsion comprises a metabolizable oil, a saponin, and a sterol. For example, an emulsion was formulated containing squalene 5, α-tocopherol 5, Tween-80 2, and water to 100 %. An adjuvant contained 3D-MPL (immunomodulator) 50, QS21 50, the above emulsion 250, phosphate-buffered solution 250 μL, and cholesterol 500 μg.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L72 ANSWER 22 OF 64 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-897527 [82] WPIDS
CROSS REFERENCE: 2003-864161 [80]
DOC. NO. CPI: C2003-254804
TITLE: New **immunostimulant** composition comprising **QS-21** and RC-529, useful for preventing or treating human diseases such as cancer, microbial infections or autoimmune diseases.
DERWENT CLASS: B04 B05 D16
INVENTOR(S): EVANS, L; MOSSMAN, S
PATENT ASSIGNEE(S): (CORI-N) CORIXA CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2003147920	A1	20030807	(200382)*		8

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 2003147920	A1 CIP of	US 2002-68171	20020204
		US 2002-177115	20020621

PRIORITY APPLN. INFO: US 2002-177115 20020621; US 2002-68171 20020204

AB US2003147920 A UPAB: 20031223
NOVELTY - An **immunostimulant** composition comprises **QS-21** and RC-529.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) treating a mammal suffering from or susceptible to a pathogenic infection, cancer or an autoimmune disorder, comprising administering to the mammal an amount of the novel composition; and
(2) enhancing the **immune** response in a mammal, comprising administering to the mammal the novel composition.
ACTIVITY - Cytostatic; Antibacterial; Antidiabetic; Nephrotropic; Antirheumatic; Antiarthritic; Antiinflammatory; **Immunosuppressive**; Dermatological.
No biological data given.
MECHANISM OF ACTION - **Vaccine.**
USE - The composition and methods are useful in preventing and/or treating various human diseases, including cancer, microbial infections and autoimmune diseases (e.g. diabetes, glomerulonephritis, psoriasis, rheumatoid arthritis or systemic lupus erythematosus).
Dwg.0/0

L72 ANSWER 23 OF 64 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-067496 [06] WPIDS

DOC. NO. CPI: C2003-017597
TITLE: Novel complex comprising **sterols** and **saponins** which are capable of contacting a genetic determinant by electrostatic or hydrophobic interaction, useful for treating humans or animals and manufacturing a medicament.
DERWENT CLASS: B01 B04 D16
INVENTOR(S): DALSGAARD, K; KIRKBY, N S
PATENT ASSIGNEE(S): (NORD-N) NORDIC VACCINE TECHNOLOGY AS; (DALS-I) DALSGAARD K; (KIRK-I) KIRKBY N S; (PHAR-N) PHAROMED AS
COUNTRY COUNT: 101
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2002080981	A2	20021017	(200306)*	EN	153
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW					
US 2003118635	A1	20030626	(200343)		
EP 1377320	A2	20040107	(200404)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002080981	A2	WO 2002-DK229	20020404
US 2003118635	A1 Provisional	US 2001-308609P	20010731
		US 2002-114957	20020404
EP 1377320	A2	EP 2002-759762	20020404
		WO 2002-DK229	20020404

FILING DETAILS:

PATENT NO	KIND	PATENT NO
EP 1377320	A2 Based on	WO 2002080981

PRIORITY APPLN. INFO: US 2001-308609P 20010731; DK 2001-560 20010404

AB WO 200280981 A UPAB: 20030124
NOVELTY - Complex (I) comprising at least one first **sterol** (S1) and/or least one second **sterol** (S2), at least one first **saponin** (N1) and/or at least one second **saponin** (N2), and optionally at least one contacting group (CG) for contacting a genetic determinant (GT) by electrostatic or hydrophobic interaction, where (S2) and (N2) are capable of contacting a GT by electrostatic or hydrophobic interaction, is new.

DETAILED DESCRIPTION - Complex (I) comprising at least one first **sterol** (S1) and/or least one second **sterol** (S2), at least one first **saponin** (N1) and/or at least one second **saponin** (N2), and optionally at least one contacting group (CG) for contacting a genetic determinant (GT) by electrostatic or hydrophobic interaction, with the proviso that CG is present when no S2 and no N2 is

present in (I). S1 and/or S2 is capable of forming a complex with at least one N1 and/or at least one N2, and N1 and/or N2 is capable of forming a complex with at least one S1 and/or at least one S2. (S2) and (N2) are capable of contacting a GT by electrostatic or hydrophobic interaction.

INDEPENDENT CLAIMS are also included for:

(1) composition (II) comprising (I) which further comprises a bioactive agent, targeting ligand for targeting (I) to a cell surface receptor moiety, a GT including a polynucleotide encoding a therapeutic protein, a polypeptide, **immunogenic** determinants, medicament for used for treating human or animal body by therapy, or a compound used for practicing a (non-invasive) diagnostic method on a human or animal body, in combination with a biodegradable microsphere or liposome;

(2) pharmaceutical composition (III) comprising (I) as described above or (II), in combination with a carrier;

(3) preparation of (I); and

(4) a kit-of-parts comprising (I), and an **immunogenic** determinant, and an antigenic determinant, where the **immunogenic** determinant is different from the antigenic determinant. The kit optionally comprises at least one genetic determinant and (I).

ACTIVITY - Cytostatic; Antipsoriatic; Neuroprotective; Antirheumatic; Antiarthritic; Antiinflammatory; Antiulcer; Dermatological; **Immunosuppressive**; Antithyroid; Antiasthmatic.

No suitable data given.

MECHANISM OF ACTION - **Immune** response modulator.

USE - (I) is useful as a medicament. (I) which further comprises a bioactive agent, targeting ligand for targeting (I) to a cell surface receptor moiety, a GT including a polynucleotide encoding a therapeutic protein, a polypeptide, **immunogenic** determinants, medicament for used for treating human or animal body by therapy, or a compound used for practicing a (non-invasive) diagnostic method on a human or animal body, and (II) are useful for treating humans or animals by therapy, where the method is:

(i) a treatment by therapy practiced on human or animal body, including a surgical method; and

(ii) a diagnostic method practiced on the human or animal body.

(I) as described above, or (II) is useful for manufacturing a medicament for treating a condition in an individual (all claimed). (I) is useful for transporting polynucleotides including DNA or RNA across cellular membranes. (I) acts as a carrier of various bioactive agents and genetic determinants, and thus is useful for introducing a polynucleotide into a patient, a predetermined region of the patient or a predetermined biological cell of the patient in order to express a gene comprised by the polynucleotide and/or to regulate the expression of genes being expressed in the biological cell in vivo and/or in vitro. v(I) is thus useful for binding any polynucleotide including DNA or RNA, peptide nucleic acids (PNAs) or locked nucleic acids. (I) is useful for promoting uptake of pharmaceutically active compounds, medicaments, and cosmetic agents, across mucosal membranes and skin surfaces. (I) and (II) are used in diagnostic methods, cosmetic treatment methods, and diagnostic methods. (I) and (II) are also used for raising a desirable **immune** response in a subject. (I) and (II) are useful for conferring a broad-based **immune** response against hyperproliferative diseases and as well as treating individuals suffering from hyperproliferative diseases such as psoriasis and cancer, where the composition comprises nucleotide sequence encoding an **immunogenic** hyperproliferating cell-associated protein. (I) and (II) are useful for prophylactically **immunizing** an individual who is predisposed to develop a particular cancer or who has had cancer and is therefore susceptible to relapse, and also for treating individuals suffering from hyperproliferative diseases. (I) and (II) are useful for treating

individuals suffering from autoimmune diseases and disorders e.g., T cell-mediated autoimmune disease such as multiple sclerosis, rheumatoid arthritis, Crohn's disease, ulcerative colitis etc; B cell-mediated autoimmune diseases such as systemic lupus erythematosus, Grave's disease, asthma, etc. (I) and (II) are useful for delivering bioactive agents to patients and/or treating conditions in a patient, for diagnosing the presence of diseased tissue in a patient, and for providing an image of an internal region of a patient.

ADVANTAGE - The polynucleotide and/or polypeptide being administered in association with (I) is not susceptible to degradation under practical circumstances or less susceptible to degradation under practical circumstances, as compared to the degradation taking place when the polynucleotide and/or polypeptide is administered in the absence of the complex.

Dwg.0/12

L72 ANSWER 24 OF 64 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-114544 [15] WPIDS
DOC. NO. CPI: C2002-035259
TITLE: Adjuvant composition useful in **immunogenic** compositions for eliciting an **immune** response, comprises highly purified saponin **QS-21** and interleukin-12, and optionally comprises 3-O-deacylated monophosphoryl **lipid** A.
DERWENT CLASS: B04 D16
INVENTOR(S): HANCOCK, G E
PATENT ASSIGNEE(S): (AMCY) AMERICAN CYANAMID CO; (AMHP) WYETH HOLDINGS CORP
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001097841	A2	20011227	(200215)*	EN	53
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001070031	A	20020102	(200230)		
EP 1305044	A2	20030502	(200331)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
KR 2003015288	A	20030220	(200340)		
BR 2001011834	A	20030708	(200364)		
CN 1437481	A	20030820	(200374)		
JP 2003535906	W	20031202	(200382)		55

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001097841	A2	WO 2001-US19805	20010621
AU 2001070031	A	AU 2001-70031	20010621
EP 1305044	A2	EP 2001-948561	20010621
		WO 2001-US19805	20010621
KR 2003015288	A	KR 2002-717426	20021220
BR 2001011834	A	BR 2001-11834	20010621
		WO 2001-US19805	20010621
CN 1437481	A	CN 2001-811650	20010621

JP 2003535906 W WO 2001-US19805 20010621
JP 2002-503325 20010621

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001070031	A	Based on	WO 2001097841
EP 1305044	A2	Based on	WO 2001097841
BR 2001011834	A	Based on	WO 2001097841
JP 2003535906	W	Based on	WO 2001097841

PRIORITY APPLN. INFO: US 2000-213143P 20000622

AB WO 200197841 A UPAB: 20020306
NOVELTY - An adjuvant composition (I) comprising a highly purified saponin (**QS-21**) and interleukin-12 (IL-12), where (I) comprises less than 1 micro g 3-O-deacylated monophosphoryl **lipid** A or does not comprise substantial 3-O-deacylated monophosphoryl **lipid** A, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an **immunogenic** composition (II) comprising at least one antigen and (I); and

(2) eliciting an **immune** response to an antigen comprising administering (II) to a vertebrate

ACTIVITY - Virucide; antibacterial; anti-HIV; fungicide; protozoacide; cytostatic.

MECHANISM OF ACTION - **Immune** response elicitor (claimed); **vaccine.** An experiment was performed to determine if **immunization** with respiratory syncytial virus F (RSV F) protein formulated with highly purified saponin (**QS-21**) and recombinant interleukin-12 (IL-12) could elicit functional serum antibody titers that were greater than those achieved after **immunization** with either adjuvant alone. Native F protein was purified by ion exchange chromatography from Vero cells and infected with the A2 strain of RSV. Native female BALB/c mice were **vaccinated** intramuscularly with natural F protein. The **vaccines** were prepared such that F protein was prepared with rIL-12 (F/rIL-12) in descending doses (1.0, 0.1, 0.001 micro g) and co-formulated with a suboptimal dose of **QS-21** (0.8 micro g). Control mice were injected with F/rIL-12 without **QS-21**, F protein admixed with 20 or 0.8 micro g **QS-21**, or F protein in phosphate buffered saline (PBS) alone. Additional control mice were **vaccinated** after experimental infection (approximately 2 multiply 106 plaque forming units (pfu)) with the A2 strain of RSV. The geometric mean serum **immunoglobulin** (Ig)G and neutralizing antibody titers were determined 2 weeks after secondary **vaccination**. The results showed that **vaccination** with an optimal dose of **QS-21** (20.0 micro g) without IL-2 generated systemic humoral and cell-mediated **immune** responses that were similar in magnitude and function to that observed after experimental infection. The anti-F protein IgG1 and IgG2a titers and complement assisted neutralizing titers were significantly elevated 2 weeks after secondary **vaccination**. **Vaccination** with F protein admixed with a suboptimal dose of **QS-21** (0.8 micro g) without IL-12, on the other hand, resulted in serum antibody titers that were significantly less when compared to F/**QS-21** (20.0 micro g). The results also demonstrated that **immunization** with F/rIL-12 (0.01-1.0 micro g) formulated in PBS alone (without **QS-21**) did not generate significant complement-assisted serum neutralizing titers. In

combination, the results indicated that **QS-21** and rIL-12 formed a potent adjuvant formulation.

USE - An **immunogenic** composition (II) comprising at least one antigen and (I), is useful for eliciting an **immune** response to an antigen, by administering (II) to the vertebrate (claimed). (I) is useful in **immunogenic** compositions containing a wide variety of antigens from a wide variety of pathogenic microorganisms including those from viruses, bacteria, fungi and parasitic microorganisms which infect humans and non-human vertebrates, or from a cancer or tumor cell. (I) is useful:

(a) in viral **vaccines** for prevention and/or treatment of disease caused by human **immunodeficiency** virus (HIV), respiratory syncytial virus;

(b) in bacterial **vaccines** for prevention and/or treatment of disease caused by H. influenzae, Streptococcus pneumoniae;

(c) in **vaccines** against fungal pathogens for prevention and/or treatment of disease caused by Candida, Blastomyces;

(d) in **vaccines** for prevention and/or treatment of disease caused by Leishmania major, Ascaris; and

(e) in **vaccines** for eliciting a therapeutic or prophylactic anti-cancer effect in a vertebrate host, for moderating responses to allergens in a vertebrate host and for preventing or treating disease characterized by amyloid deposition in a vertebrate host.

(II) is useful for eliciting functional cell-mediated and humoral **immune** responses against an antigen.

ADVANTAGE - In (I), IL-12 and **QS-21** together form a potent adjuvant combination for eliciting functional cell-mediated and humoral **immune** responses against antigens. This synergy allows a reduction in the total adjuvant amount and/or a reduction in the amount of either adjuvant component which may have undesirable effects when used alone.

Dwg.0/1

L72 ANSWER 25 OF 64 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-075044 [10] WPIDS
DOC. NO. CPI: C2002-022288
TITLE: Synergistic adjuvant composition, useful in **vaccines** against infection, cancer and autoimmune diseases, contains **QS-21** and RC-529.
DERWENT CLASS: B04 D16
INVENTOR(S): EVANS, L; MOSSMAN, S
PATENT ASSIGNEE(S): (CORI-N) CORIXA CORP
COUNTRY COUNT: 96
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001078777	A2	20011025	(200210)*	EN	19
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2001051622	A	20011030	(200219)		
EP 1385541	A1	20040204	(200410)	EN	
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE TR					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001078777	A2	WO 2001-US12182	20010413
AU 2001051622	A	AU 2001-51622	20010413
EP 1385541	A1	EP 2001-925021	20010413
		WO 2001-US12182	20010413

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001051622	A	Based on	WO 2001078777
EP 1385541	A1	Based on	WO 2001078777

PRIORITY APPLN. INFO: US 2000-196846P 20000413

AB WO 200178777 A UPAB: 20020213

NOVELTY - **Immunostimulant** composition (A) comprising **QS -21** and RC-529 (2-((R)-3-tetradecanoyloxytetradecanoylamino)ethy 1-2-deoxy-4-O-phosphono-3-O- ((R)-3-tetradecanoyloxytetradecanoyl)-2-((R)-3-tetradecanoyloxytetradecanoylamino)- beta -D-glucopyranoside triethylammonium salt), is new.

ACTIVITY - Virucide; anti-HIV (human **immunodeficiency** virus); antibacterial; tuberculostatic; protozoacide; fungicide; cytostatic; **immunosuppressive.**

MECHANISM OF ACTION - Stimulation of an **immune** response.

USE - (A), optionally when combined with an antigen or DNA that encodes it, are used to treat, or prevent, pathogenic infections (viral, bacterial, fungal or protozoal), or a wide range of cancers and autoimmune diseases.

ADVANTAGE - **QS-21** and RC-529 synergistically increase the **immune** response to co-administered antigens, particularly they induce cytotoxic T lymphocytes (CTL) from recombinant proteins (which normally generate only antibody and helper cell responses). They also increase production of interferon gamma . C57BL/6 mice were **immunized** (weeks 0, 3 and 7), subcutaneously, with 5 micro g of the recombinant polypeptide antigen rDPV of Mycobacterium tuberculosis, formulated with 10 micro g RC-529, 10 micro g **QS-21**, or 10 micro g of both adjuvants. Two weeks after the last injection, spleen cells were isolated, stimulated with EL-4 cells, expressing rDPV, then after a further 13 days, tested for CTL activity against EL-4 cells. Specific lysis was 10.4 %; 9.2 % and 32.7 %. Corresponding figures for secretion of interferon gamma (in pg/ml) were 539; 832 and 34294.

Dwg.0/0

L72 ANSWER 26 OF 64 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2001-663016 [76] WPIDS

DOC. NO. CPI: C2001-194795

TITLE: Producing a polypeptide delivery system useful in a **vaccine** to treat infection by mixing together the polypeptide, **cholesterol, saponin,** and a **phospholipid** in presence of a nonionic detergent and a second detergent.

DERWENT CLASS: B04

INVENTOR(S): SANYAL, G; SHAPIRO, A

PATENT ASSIGNEE(S): (ASTR) ASTRAZENECA AB

COUNTRY COUNT: 95

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2001076625 A1 20011018 (200176)* EN 17
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
AU 2001048954 A 20011023 (200213)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001076625 A1		WO 2001-SE799	20010409
AU 2001048954 A		AU 2001-48954	20010409

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001048954 A	Based on	WO 2001076625

PRIORITY APPLN. INFO: GB 2000-8879 20000412

AB WO 200176625 A UPAB: 20011227

NOVELTY - Production of a polypeptide delivery system comprising an **immune** stimulating complex (ISCOM) coupled to a polypeptide, involves: mixing the polypeptide, **cholesterol**, a **saponin**, and a **phospholipid** in the presence of a nonionic detergent and a second detergent to form a solution; and removing the detergent from the mixture to form the ISCOM.

DETAILED DESCRIPTION - Production of a polypeptide delivery system comprising an **immune** stimulating complex (ISCOM) coupled to a polypeptide, involves: (a) mixing the polypeptide, **cholesterol**, a **saponin**, and a **phospholipid** in the presence of a nonionic detergent and a second detergent to form a solution; and (b) removing the detergent from the mixture to form the ISCOM. The second detergent is of formula Z-X-Y.

X = optionally substituted hydrocarbon moiety having at least 8 aliphatic carbon atoms and is uncharged;

Y = changed moiety;

Z = rest of the detergent moiety.

ACTIVITY - Anti-bacterial. A polypeptide delivery system (A) was prepared by mixing (parts by volume) **Saponin** 703 (4), **lipid**/nOG solution (1), TOPPS solution (1), buffer and His-HOP 38(-11) (comprising a fully defined 289 amino acid sequence as given in the specification) (0.4 mg/ml). The resulting mixture was dialyzed for 2 days against buffer (1000 volumes) with a moderate rate of stirring at room temperature. Mice were challenged with H.pylori SS1 (106 CFU) by gavage in a volume of 200 mu l. Two weeks after infection, each mouse received intranasally four weekly doses of 100 mu g of (A) or a comparative without the His-HOP38 (-11). The mice were sacrificed 2 weeks after the fourth dose and the therapeutic treatment of pre-existing H. pylori infection was assayed using the CFU assay. For each group, half of the total volume of the formulation was administered into each nostril. The formulations were diluted. For infection of H.pylori (14300 plus or minus 5850 CFU), the protection was 0.05 as described by Wilcoxon Rank Sum test which indicated that a significant protection. For infection of H.pylori (14300 plus or minus 5850 CFU), the protection was not given.

MECHANISM OF ACTION - None given.

USE - As a medicament for the manufacture of a **vaccine** for administration to a mammalian patients, to treat and prevent Helicobacter pylori infection in the patients (claimed).

ADVANTAGE - The method has a broad applicability to polypeptides, including polypeptides that are unsuited to prior art processes.

Dwg.0/2

L72 ANSWER 27 OF 64 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2002-025884 [03] WPIDS
DOC. NO. CPI: C2002-007215
TITLE: Production of a polypeptide delivery system useful as a medicament comprises mixing together the polypeptide, **cholesterol, saponin,** and a **phospholipid** with a polar head group, in the presence of a detergent.
DERWENT CLASS: B04
INVENTOR(S): SANYAL, G; SHAPIRO, A
PATENT ASSIGNEE(S): (ASTR) ASTRAZENECA AB
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001076623	A1	20011018	(200203)*	EN	48

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001047031 A 20011023 (200213)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001076623	A1	WO 2001-SE800	20010409
AU 2001047031	A	AU 2001-47031	20010409

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001047031	A	Based on	WO 2001076623

PRIORITY APPLN. INFO: GB 2000-8877 20000412

AB WO 200176623 A UPAB: 20020114

NOVELTY - A process for production of a polypeptide delivery system (I) comprising an **immune** stimulating complex (ISCOM) coupled to a polypeptide of Helicobacter pylori or its antigenic fragment comprises: mixing the polypeptide, **cholesterol**, a **saponin**, and a **phospholipid** having a polar head group; and removing the detergent from the mixture to form ISCOM.

DETAILED DESCRIPTION - A process for production of a polypeptide delivery system comprising an **immune** stimulating complex (ISCOM) coupled to a polypeptide of Helicobacter pylori or its antigenic fragment comprises:

(a) mixing the polypeptide, **cholesterol, saponin,** and a **phospholipid** having a polar head group, in the presence of a detergent to form a solution; and

(b) (b) removing the detergent from the mixture so that the ISCOM forms. The head group of the **phospholipid** has a net charge and a terminal charge.

Provided that the following processes are not included:

(i) a process carried out at pH 8 where the polypeptide is Helicobacter pylori HpE protein, cardiolipin or diphosphoryl **lipid** A (DPL) or dipalmitoylphosphatidyl glycerol, which is used as a sole **phospholipid** and the **saponin** which is provided by **saponin** preparation (D) comprising (weight%) Fraction A (50 - 90) of Quil A and Fraction C (50 - 10) of Quil A;

(ii) a process carried out at pH 7.2 where the polypeptide is Helicobacter pylori HpC protein, or (DPL) as a sole **phospholipid** and the **saponin** which is provided by (D); and

(iii) a process carried out at pH 7.2 where the polypeptide is Helicobacter pylori HpE protein that is tagged with 6 histidine residues or 6 histidine residues and 6 lysine residues, dipalmitoylphosphatidylcholine and dipalmitoyl-rac-glycerol-3(8-(3,6-dioxy)octyl-1-amino-N,N-diacetic acid, which is used as a sole **phospholipid** and the **saponin** provided by (D).

An INDEPENDENT CLAIM is also included for use of the system (I) obtained by the process, in the manufacture of a **vaccine**.

ACTIVITY - Antibacterial.

No biological data given.

MECHANISM OF ACTION - None given.

USE - As a medicament for the manufacture of a **vaccine** for administration to a mammalian patient, to treat or prevent Helicobacter pylori infection in the patient (claimed).

ADVANTAGE - The method has a broad applicability to polypeptides, including polypeptides that are unsuited to prior art processes.

Dwg.0/4

L72 ANSWER 28 OF 64 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2001-146972 [15] WPIDS
DOC. NO. CPI: C2001-043422
TITLE: New plasmid for expressing peptidoglycan-associated lipoproteins, especially **lipidated** P6 protein from Haemophilus influenzae for use as a **vaccine** against bacterial infection.
DERWENT CLASS: B04 D16
INVENTOR(S): METCALF, B J
PATENT ASSIGNEE(S): (AMCY) AMERICAN CYANAMID CO
COUNTRY COUNT: 92
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001000790	A1	20010104	(200115)*	EN	50
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
AU 2000057534	A	20010131	(200124)		
BR 2000011804	A	20020319	(200228)		
EP 1192242	A1	20020403	(200230)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
KR 2002039270	A	20020525	(200275)		
CN 1358227	A	20020710	(200278)		

JP 2003503043 W 20030128 (200309) 45
MX 2001013253 A1 20020601 (200365)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001000790	A1	WO 2000-US17020	20000620
AU 2000057534	A	AU 2000-57534	20000620
BR 2000011804	A	BR 2000-11804	20000620
		WO 2000-US17020	20000620
EP 1192242	A1	EP 2000-942996	20000620
		WO 2000-US17020	20000620
KR 2002039270	A	KR 2001-716321	20011219
CN 1358227	A	CN 2000-809423	20000620
JP 2003503043	W	WO 2000-US17020	20000620
		JP 2001-506784	20000620
MX 2001013253	A1	WO 2000-US17020	20000620
		MX 2001-13253	20011218

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000057534	A	Based on	WO 2001000790
BR 2000011804	A	Based on	WO 2001000790
EP 1192242	A1	Based on	WO 2001000790
JP 2003503043	W	Based on	WO 2001000790
MX 2001013253	A1	Based on	WO 2001000790

PRIORITY APPLN. INFO: US 1999-141061P 19990625
AB WO 200100790 A UPAB: 20010317
NOVELTY - A plasmid (I) comprising a tightly regulated promoter which is operatively linked to an isolated and purified DNA sequence encoding a peptidoglycan-associated lipoprotein (PAL) of gram-negative bacteria, where PAL is expressed in lipidated form, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(1) a bacterial host cell transformed, transduced, or transfected with (I).

(2) a method of producing a recombinant lipidated PAL, comprising:

(a) transforming, transducing or transfecting a bacterial host cell with the plasmid described above; and

(b) culturing the host cell under conditions which permit expression of the lipidated recombinant PAL by the cell;

(3) an antigenic composition comprising lipidated recombinant PAL. The composition elicits a protective **immune** response in a mammalian host; and

(4) a method of **immunizing** against a gram-negative bacterium, comprising administering an **immunogenic** amount of the composition described in (2) to a mammalian host.

ACTIVITY - Antibacterial.
No data given.

MECHANISM OF ACTION - **Vaccine.**
No data given.

USE - The plasmid is useful for transfecting host cells with DNA which encodes PALs of gram-negative bacteria, particularly H. influenzae. The lipidated PAL produced can be used as an **immunogen** in antigenic compositions against gram-negative bacteria and can thus be used in prevention of bacterial infections such as pneumonia and meningitis.

ADVANTAGE - Lipidated P6 protein (i.e. P6 protein modified at the

terminal cysteine with lipids) produced by host cells transfected with the above plasmid is much more **immunogenic** than the non-lipidated form of P6 previously used. This allows much lower doses to be used to **immunize** humans and makes the lipidated protein a more commercially viable candidate for use in antigenic compositions.
Dwg.0/3

L72 ANSWER 29 OF 64 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1999-204961 [17] WPIDS
DOC. NO. CPI: C1999-059644
TITLE: Oil in water **emulsions** containing **saponins** - useful in **vaccine** formulations.
DERWENT CLASS: B04 B05 B07 D16
INVENTOR(S): GARCON, N; MOMIN, P M C A F
PATENT ASSIGNEE(S): (SMIK) SMITHKLINE BEECHAM BIOLOGICALS; (GLAX) GLAXOSMITHKLINE BIOLOGICALS SA
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9911241	A1	19990311	(199917)*	EN	72
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW					
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW					
AU 9911456	A	19990322	(199931)		
EP 1009382	A1	20000621	(200033)	EN	
R: BE CH DE ES FR GB IT LI NL					
JP 2001514208	W	20010911	(200167)		90
EP 1279401	A1	20030129	(200310)	EN	
R: BE CH DE ES FR GB IT LI NL					
US 2003095974	A1	20030522	(200336)		
EP 1009382	B1	20030618	(200341)	EN	
R: BE CH DE ES FR GB IT LI NL					
DE 69815692	E	20030724	(200356)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9911241	A1		WO 1998-EP5715	19980902
AU 9911456	A		AU 1999-11456	19980902
EP 1009382	A1		EP 1998-954264	19980902
			WO 1998-EP5715	19980902
JP 2001514208	W		WO 1998-EP5715	19980902
			JP 2000-508344	19980902
EP 1279401	A1	Div ex	EP 1998-954264	19980902
			EP 2002-18002	19980902
US 2003095974	A1	Cont of	WO 1998-EP5715	19980902
		Cont of	US 2000-486997	20000731
			US 2002-139815	20020506
EP 1009382	B1		EP 1998-954264	19980902
			WO 1998-EP5715	19980902
		Related to	EP 2002-18002	19980902
DE 69815692	E		DE 1998-615692	19980902
			EP 1998-954264	19980902

WO 1998-EP5715 19980902

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9911456	A	Based on	WO 9911241
EP 1009382	A1	Based on	WO 9911241
JP 2001514208	W	Based on	WO 9911241
EP 1279401	A1	Div ex	EP 1009382
EP 1009382	B1	Related to	EP 1279401
		Based on	WO 9911241
DE 69815692	E	Based on	EP 1009382
		Based on	WO 9911241

PRIORITY APPLN. INFO: GB 1997-20982 19971002; GB 1997-18902 19970905

AB WO 9911241 A UPAB: 19990503

NOVELTY - A new composition comprises an oil (which is metabolizable) in water emulsion and a **saponin** with a ratio of oil:**saponin** of 1:1 to 200:1. DETAILED DESCRIPTION - INDEPENDENT CLAIMs are also included for: (1) a **vaccine** composition comprising the novel composition and an antigen or antigenic preparation; and (2) a method of stabilising a **saponin** present in the novel composition, by addition of a **sterol** into the oil phase of the oil in water emulsion.

ORGANIC CHEMISTRY - Preferred Composition: The ratio of oil: **saponin** is preferably 1:1 to 100:1, especially 48:1. The **saponin** is preferably QuilA or a derivative such as QS21 and the oil is preferably squalene. The composition may further include a **sterol**, preferably **cholesterol**, and an **immunomodulator**, especially 3D-MPL or alpha -tocopherol. The ratio of QS21:3D-MPL is preferably 1:10 to 10:1, especially 1:1 to 1:2.5. The ratio QS21:**cholesterol** is preferably 1:1 to 1:20. The antigen is preferably prepared from Human **Immunodeficiency** Virus, Herpes Simplex Virus type 1, Herpes Simplex Virus type 2, Human Cytomegalovirus, Hepatitis A, B, C or E, Respiratory Syncitial Virus, Human Papilloma Virus, Influenza Virus, Salmonella, Neisseria, Borrelia, Chlamydia, Bordetella, TB, EBV, Plasmodium, Toxoplasma or a combination of Malaria antigens RTS,S and TRAP. The antigen may be derived from a tumor or host derived antigen.

USE - The composition is useful for treating diseases. ACTIVITY - None given. MECHANISM OF ACTION - The **vaccine** invokes a cytolytic T-cell response and stimulates interferon- gamma production.

ADVANTAGE - Inclusion of the **sterol** stabilises the **saponin**.

Dwg.0/0

L72 ANSWER 30 OF 64 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1996-085830 [09] WPIDS
DOC. NO. CPI: C1996-027592
TITLE: Foot-and-mouth disease **vaccine** synthesis - using **saponin** and **cholesterol** mixture as emulsifier, adding former to inactivated antigen and latter to oil-based phase, then combining.
DERWENT CLASS: B04 C06 D16
INVENTOR(S): DUDNIKOV, S A; GUSEV, A A; GUSEVA, E V
PATENT ASSIGNEE(S): (FOOT-R) FOOT & MOUTH DISEASE INST
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
SU 991634	A1	19950609	(199609)*		6

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
SU 991634	A1	SU 1980-2935342	19800605

PRIORITY APPLN. INFO: SU 1980-2935342 19800605
AB SU 991634 A UPAB: 19960305
A foot-and-mouth **vaccine** with enhanced **immunogenicity** can be obtd. by combining an aqueous phase containing the virus antigen emulsifiers. A mixture of **saponin** and **cholesterol** (5-7 and 0.5-1.0 weight% respectively w.r.t. **vaccine**) is used as the emulsifier; the **saponin** is first added to the inactivated antigen and the **cholesterol** to the oil phase prior to emulsification.
USE - The method is used in biology and veterinary science.
ADVANTAGE - A **vaccine** of increased **immunogenicity** can be obtd.
Dwg.0/0

L72 ANSWER 31 OF 64 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1995-022469 [03] WPIDS
DOC. NO. CPI: C1995-010369
TITLE: **Vaccine** containing respiratory syncytial virus protein - and specific adjuvant e.g. **QS-21**, provides improved humoral and cellular responses.
DERWENT CLASS: B04 D16
INVENTOR(S): FRENCHICK, P J; HANCOCK, G E; SPEELMAN, D J
PATENT ASSIGNEE(S): (AMCY) AMERICAN CYANAMID CO; (FREN-I) FRENCHICK P J; (HANC-I) HANCOCK G E; (SPEE-I) SPEELMAN D J
COUNTRY COUNT: 25
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9427636	A1	19941208	(199503)*	EN	39
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE					
W: AU CA FI JP NO RU US					
AU 9469571	A	19941220	(199512)		
FI 9505667	A	19960112	(199613)		
NO 9504786	A	19960123	(199613)		
EP 705109	A1	19960410	(199619)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
JP 08510749	W	19961112	(199708)		37
AU 676340	B	19970306	(199718)		
US 5723130	A	19980303	(199816)		12
BR 1100802	A3	19980512	(199828)		
EP 705109	B1	20001004	(200050)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
DE 69426077	E	20001109	(200064)		
ES 2150493	T3	20001201	(200105)		
RU 2160119	C2	20001210	(200110)		
EP 705109	B2	20040102	(200406)	EN	

R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9427636	A1	WO 1994-US5833	19940524
AU 9469571	A	AU 1994-69571	19940524
		WO 1994-US5833	19940524
FI 9505667	A	WO 1994-US5833	19940524
		FI 1995-5667	19951124
NO 9504786	A	WO 1994-US5833	19940524
		NO 1995-4786	19951124
EP 705109	A1	EP 1994-918109	19940524
		WO 1994-US5833	19940524
JP 08510749	W	WO 1994-US5833	19940524
		JP 1995-500899	19940524
AU 676340	B	AU 1994-69571	19940524
US 5723130	A	WO 1994-US5833	19940524
		US 1996-553332	19960916
BR 1100802	A3	BR 1997-1100802	19970512
EP 705109	B1	EP 1994-918109	19940524
		WO 1994-US5833	19940524
DE 69426077	E	DE 1994-626077	19940524
		EP 1994-918109	19940524
		WO 1994-US5833	19940524
ES 2150493	T3	EP 1994-918109	19940524
RU 2160119	C2	WO 1994-US5833	19940524
		RU 1995-122391	19940524
EP 705109	B2	EP 1994-918109	19940524
		WO 1994-US5833	19940524

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9469571	A	Based on	WO 9427636
EP 705109	A1	Based on	WO 9427636
JP 08510749	W	Based on	WO 9427636
AU 676340	B	Previous Publ.	AU 9469571
		Based on	WO 9427636
US 5723130	A	Based on	WO 9427636
EP 705109	B1	Based on	WO 9427636
DE 69426077	E	Based on	EP 705109
		Based on	WO 9427636
ES 2150493	T3	Based on	EP 705109
RU 2160119	C2	Based on	WO 9427636
EP 705109	B2	Based on	WO 9427636

PRIORITY APPLN. INFO: US 1993-67855 19930525; US 1996-553332 19960916

AB WO 9427636 A UPAB: 19950126

Vaccine comprising a respiratory syncytial virus (RSV) protein (I), or its **immunological** fragment, and as an adjuvant 1 **QS-21**, monophosphoryl **lipid** A or 3-deacylated monophosphoryl **lipid** A(3D-MPL) in a vehicle, is new.

USE - The **vaccines** are used to prevent infections (or disease symptoms) caused by RSV. 0.1-100 (especially 5-25) mug (I) per dose, plus 1-100 (especially 20-50) mug adjuvant. **Vaccines** are administered by injection or intranasally.

ADVANTAGE - Compared with the use of alum, these adjuvants give significantly better humoral and cellular **immunogenicity**, and prevent formation of syncytia in virally infected cells. They induce antibodies able to neutralise RSV of both A and B sub-types and may allow formulation of **vaccines** with reduced (I) content.
Dwg.0/1

L72 ANSWER 32 OF 64 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1992-433344 [52] WPIDS
DOC. NO. CPI: C1992-192346
TITLE: Carrier for admin. of a pharmaceutically active substance comprises matrix of a complex of a **sterol** e.g. **cholesterol**, and one or more **saponin**(s) having inert structure.
DERWENT CLASS: B01
INVENTOR(S): LOEVGREN, K; MOREIN, B; LOVGREN, K
PATENT ASSIGNEE(S): (KABI) KABI PHARMACIA AB; (BRTE-N) BRITISH TECHNOLOGY GROUP LTD; (ISCO-N) ISCOVENT AB
COUNTRY COUNT: 37
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9221331	A1	19921210	(199252)*	EN	38
RW: AT BE CH DE DK ES FR GB GR IT LU MC NL OA SE					
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK LU MG MN MW NL NO PL RO RU SD SE US					
SE 9101665	A	19921201	(199304)		
AU 9219251	A	19930108	(199315)		
FI 9305314	A	19931129	(199406)		
EP 587659	A1	19940323	(199412)	EN	
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE					
NO 9304315	A	19940126	(199414)		
JP 07500084	W	19950105	(199511)		
SE 502569	C2	19951113	(199551)		
US 5603958	A	19970218	(199713)		15
EP 587659	B1	19970507	(199723)	EN	22
R: AT BE CH DE DK ES FR GB GR IT LI LU MC NL SE					
DE 69219600	E	19970612	(199729)		
AU 680807	B	19970814	(199741)		
ES 2103946	T3	19971001	(199746)		
CA 2103447	C	19990316	(199929)		
NO 306539	B1	19991122	(200002)		
KR 227302	B1	19991101	(200110)		
FI 110408	B1	20030131	(200319)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9221331	A1	WO 1992-SE367	19920601
SE 9101665	A	SE 1991-1665	19910531
AU 9219251	A	AU 1992-19251	19920601
		WO 1992-SE367	19920601
FI 9305314	A	WO 1992-SE367	19920601
		FI 1993-5314	19931129
EP 587659	A1	EP 1992-911403	19920601
		WO 1992-SE367	19920601
NO 9304315	A	WO 1992-SE367	19920601
		NO 1993-4315	19931129

JP 07500084	W		JP 1992-511348	19920601
			WO 1992-SE367	19920601
SE 502569	C2		SE 1991-1665	19910531
US 5603958	A	Cont of	US 1994-142377	19940330
			US 1995-455403	19950531
EP 587659	B1		EP 1992-911403	19920601
			WO 1992-SE367	19920601
DE 69219600	E		DE 1992-619600	19920601
			EP 1992-911403	19920601
			WO 1992-SE367	19920601
AU 680807	B		AU 1992-19251	19920601
ES 2103946	T3		EP 1992-911403	19920601
CA 2103447	C		CA 1992-2103447	19920601
NO 306539	B1		WO 1992-SE367	19920601
			NO 1993-4315	19931129
KR 227302	B1		WO 1992-SE367	19920601
			KR 1993-703641	19931129
FI 110408	B1		WO 1992-SE367	19920601
			FI 1993-5314	19931129

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9219251	A	Based on	WO 9221331
EP 587659	A1	Based on	WO 9221331
JP 07500084	W	Based on	WO 9221331
EP 587659	B1	Based on	WO 9221331
DE 69219600	E	Based on	EP 587659
		Based on	WO 9221331
AU 680807	B	Previous Publ.	AU 9219251
		Based on	WO 9221331
ES 2103946	T3	Based on	EP 587659
NO 306539	B1	Previous Publ.	NO 9304315
FI 110408	B1	Previous Publ.	FI 9305314

PRIORITY APPLN. INFO: SE 1991-1665 19910531

AB WO 9221331 A UPAB: 19950314

The use of an inert, structive-giving, deadjuvanted matrix of a complex of a **sterol** and one or more **saponins**, as a carrier for admin, of a pharmaceutically active substance, not intended for **immunisation** is new. The matrix has an annular basic structive which can form spheric nano particles with a narrow size distribution. The **sterol** is e.g. **cholesterol**.

The matrix may also comprise one or more other lipids, especially phospholipids e.g. phosphatidylethandamine or phosphatidylcholin. The carrier particles are in the size range of 50 to 50 mm, especially about 50 mm. The **saponins** may be B4b or LT15 opt. in combination in the matrix with B2 or Lt17. The matrix may in addition comprise one or more adjuvant active **saponins**. The pharmaceutically active substance is pref. CoQ10 or amfotericin B and is connected to the matrix by covalent or hydrophobic bonds.

USE/ADVANTAGE - It has recently been discovered that nano particles can penetrate the microns membrane of the intestines, so a good absorption should be obtained after oral admin. of drugs which are sparingly soluble. Pharmaceutical carriers in the form of injectable nano particles are useful for admin of drugs to tumours and for sustained release of drugs. Owing to its stability, the matrix normally shows a consisderably lower toxicity than the sum of the included component

Dwg.0/11

Dwg.0/11

L72 ANSWER 33 OF 64 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1988-272249 [39] WPIDS
DOC. NO. CPI: C1988-121135
TITLE: New complex of **saponin** with **phospholipid**, opt. containing **sterol** useful in cosmetic, pharmaceutical and dermatological compsn., with reduced toxicity, high stability etc..
DERWENT CLASS: B04 D21
INVENTOR(S): BOMBARDELL, E; PATRI, G F; POZZI, R; BOMBARDELLI, E; PATRI, G
PATENT ASSIGNEE(S): (INDE-N) INDENA SPA
COUNTRY COUNT: 15
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 283713	A	19880928	(198839)*	EN	9
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
JP 63277691	A	19881115	(198851)		
IT 1203515	B	19890215	(199125)		
US 5118671	A	19920602	(199225)		3
US 5147859	A	19920915	(199240)		3
US 5166139	A	19921124	(199250)		3
EP 283713	B1	19930811	(199332)	EN	11
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
DE 3883035	G	19930916	(199338)		
ES 2058151	T3	19941101	(199444)		
JP 2768465	B2	19980625	(199830)		7

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 283713	A		EP 1988-102321	19880218
JP 63277691	A		JP 1988-43269	19880225
US 5118671	A	Cont of	US 1988-158577	19880222
		CIP of	US 1990-514126	19900425
			US 1990-629843	19901219
US 5147859	A	Cont of	US 1988-158577	19880222
		CIP of	US 1990-514126	19900425
			US 1991-641291	19910115
US 5166139	A	Cont of	US 1988-158577	19880222
		CIP of	US 1990-514126	19900425
			US 1991-643791	19910118
EP 283713	B1		EP 1988-102321	19880218
DE 3883035	G		DE 1988-3883035	19880218
			EP 1988-102321	19880218
ES 2058151	T3		EP 1988-102321	19880218
JP 2768465	B2		JP 1988-43269	19880225

FILING DETAILS:

PATENT NO	KIND		PATENT NO
DE 3883035	G	Based on	EP 283713
ES 2058151	T3	Based on	EP 283713
JP 2768465	B2	Previous Publ.	JP 63277691

PRIORITY APPLN. INFO: IT 1987-19496 19870226
AB EP 283713 A UPAB: 19930923

Phospholipid complexes (A) of **saponins** (I), themselves opt. complexed with **cholesterol** or phytasterols, are new.

The **phospholipid** (II): (I) ratio is 0.5-2, especially about 1. Most pref. are equimolar complexes of soya phosphatidyl choline with exim/**cholesterol** or beta-**sitosterol**.

USE/ADVANTAGE - (A) are useful in pharmaceutical, dermatological and cosmetic compsns. In these complexes, (I) are effective when given orally or topically; have high stability and better activity and tolerance. The complexes are lipophilic so will dissolve in a polar and aprotic solvents which will not dissolve the individual components. (I) are known to have a wide range of biological activity, e.g. antioedema, vasotonic, vasoprotective, **immunomodulating**, cardiovascular, CNS, enzyme- or hormone- inhibiting activities.

0/0

L72 ANSWER 34 OF 64 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1987-122641 [17] WPIDS
CROSS REFERENCE: 1986-120682 [19]
DOC. NO. CPI: C1987-051023
TITLE: Preparation of **immunogenic** complex containing antigens with hydrophobic domains - includes addition of **lipid**(s) to prevent formation of **aggregates**.
DERWENT CLASS: B04 D16
INVENTOR(S): MOREIN, B
PATENT ASSIGNEE(S): (MORE-I) MOREIN B
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8702250	A	19870423	(198717)*	EN	45
RW: AT BE CH DE FR GB IT LU					
W: AU DK FI JP					
ZA 8607792	A	19870415	(198727)		
AU 8664752	A	19870505	(198730)		
NO 8702484	A	19870817	(198738)		
EP 242380	A	19871028	(198743)	EN	
R: AT BE CH DE FR GB IT LI LU NL SE					
DK 8703029	A	19870814	(198809)		
FI 8702647	A	19870615	(198810)		
JP 63501078	W	19880421	(198822)		
ES 2002532	A	19880816	(198927)		
CA 1275246	C	19901016	(199047)		
DE 3678567	G	19910508	(199120)		
EP 242380	B	19910403	(199148)		
R: AT BE CH DE FR GB IT LI LU NL SE					
US 5254339	A	19931019	(199343)		14
JP 07051514	B2	19950605	(199527)		14

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8702250	A	WO 1986-SE480	19861016
ZA 8607792	A	ZA 1986-7792	19861014
EP 242380	A	EP 1986-906026	19861016
JP 63501078	W	JP 1986-505483	19861016

ES 2002532	A	ES 1986-2624	19861016
US 5254339	A	WO 1986-SE480	19861016
		US 1987-70920	19870601
JP 07051514	B2	JP 1986-505483	19861016
		WO 1986-SE480	19861016

FILING DETAILS:

PATENT NO	KIND		PATENT NO
US 5254339	A	Based on	WO 8702250
JP 07051514	B2	Based on	JP 63501078
		Based on	WO 8702250

PRIORITY APPLN. INFO: EP 1985-850326 19851016; EP 1986-906026 19861016

AB WO 8702250 A UPAB: 19950721

In the preparation of an **immunogenic** complex containing antigens or antigenic determinants with hydrophobic domains, viruses, mycoplasmas, bacteria, parasites, animal cells, antigens (Ag) or antigenic determinants (AD) with hydro-phobic domains are mixed with 1 or more solubilising agents (I) so that complexes are formed with (I), the Ag or AD are separated from (I) in the presence of, or are separated from (I) and directly transferred to a glycoside solution, containing 1 or more glycosides (II) with hydrophobic and hydrophilic domains in a concentration of at least the critical micellular concentration, thereby forming a protein complex which is isolated and purified, characterised in that lipids are added before the complex is isolated and purified.

Pref. the lipids are chosen from membrane lipids in animal or plant cells such as fats, glycerol ethers, waxes, phospholipids, sulpholipids, glycolipids and isoprenoids and the lipids are added in a molar ratio of **lipid** to Ag or AD of at least 0.1.

USE/ADVANTAGE - Addition of the lipids when preparing the complex prevents the formation of aggregates, i.e. micelles. Thecomplex can be used for specific **immuno**-stimulation in humans and animals. They can thus be used for **immuno**-modulation and diagnostics and as **vaccines** against diseases caused by bacteria, viruses, mycoplasmas and parasites and for producing antibodies. They can also be used as analytical reagents and carrier for substances that one wants to increase the **immunogenicity** of.

Dwg.0/0

Dwg.0/0

L72 ANSWER 35 OF 64 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 9

ACCESSION NUMBER: 96007423 EMBASE
DOCUMENT NUMBER: 1996007423
TITLE: Isolation and quantification of **Quillaja** saponaria Molina saponins and lipids in iscom-matrix and iscoms.
AUTHOR: Behboudi S.; Morein B.; Ronnberg B.
CORPORATE SOURCE: Swedish Univ. Agricultural Sciences, Department of Vet. Microbiology, Section of Virology, Box 585 Biomedicum, 751 23 Uppsala, Sweden
SOURCE: Vaccine, (1995) 13/17 (1690-1696).
ISSN: 0264-410X CODEN: VACCDE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Pharmacology

037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In the iscom, multiple copies of antigen are attached by hydrophobic interaction to a matrix which is built up by **Quillaja** triterpenoid saponins and lipids. Thus, the iscom presents antigen in multimeric form in a small particle with a built-in adjuvant resulting in a highly immunogenic antigen formulation. We have designed a chloroform-methanol-water extraction procedure to isolate the triterpenoid saponins and lipids incorporated into iscom-matrix and iscoms. The triterpenoids in the triterpenoid phase were quantitated using orcinol sulfuric acid detecting their carbohydrate chains and by HPLC. The cholesterol and phosphatidylcholine in the lipid phase were quantitated by HPLC and a commercial colorimetric method for the cholesterol. The quantitative methods showed an almost total separation and recovery of triterpenoids and lipids in their respective phases, while protein was detected in all phases after extraction. The protein content was determined by the method of Lowry and by amino acid analysis. Amino acid analysis was shown to be the reliable method of the two to quantitate proteins in iscoms. In conclusion, simple, reproducible and efficient procedures have been designed to isolate and quantitate the triterpenoids and lipids added for preparation of iscom-matrix and iscoms. The procedures described should also be useful to adequately define constituents in prospective vaccines.

L72 ANSWER 36 OF 64 EMBASE
on STN DUPLICATE 11
ACCESSION NUMBER: 91099758 EMBASE
DOCUMENT NUMBER: 1991099758
TITLE: On the structure of immune-stimulating saponin-lipid complexes (iscoms).
AUTHOR: Kersten G.F.A.; Spiekstra A.; Beuvery E.C.; Crommelin D.J.A.
CORPORATE SOURCE: Dept. Inactivated Viral Vacc., Nat. Inst. Public Health, Environmental Protection RIVM, P.O. Box 1,3720 BA Bilthoven, Netherlands
SOURCE: Biochimica et Biophysica Acta - Biomembranes, (1991) 1062/2 (165-171).
ISSN: 0005-2736 CODEN: BBBMBS
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Immune-stimulating complexes (iscoms) are stable complexes of cholesterol, phospholipid and Quil A, a triterpene saponin mixture in the size range from 400 to 100 nm. They can be used as antigen carriers in subunit vaccines. In this paper it is demonstrated that iscoms are rigid, negatively charged vesicles in which small water soluble molecules like carboxyfluorescein cannot be retained. The negative zeta-potential prevents iscoms from aggregation. The chemical composition of iscoms in one dispersion varied considerably. A typical example of the composition of iscoms is cholesterol/phospholipid/Quil A = 1.0:1.2:6.2 by weight for the iscom matrix, that is iscoms without antigen, and 1.0:1.3:5.1 for antigen-containing iscoms. A hypothetical model for the structure of the iscom matrix and related structures is presented, based on analytical chemical, physico-chemical and electronmicroscopic data. In this model iscoms are considered to be multi-micellar structures, shaped and

stabilized by hydrophobic interactions, electrostatic repulsion, steric factors and possibly hydrogen bonds. The individual micelles are relatively flat, ring-shaped structures, the center offering space for one of the two bulky sugar chains of the saponins.

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ACCESSION NUMBER: 2003440622 EMBASE
TITLE: Third meeting on Novel Adjuvants Currently in or Close to Clinical Testing World Health Organization - Organisation Mondiale de la Sante, Fondation Merieux, Annecy, France, 7-9 January 2002.
AUTHOR: Engers H.; Kieny M.P.; Malhotra P.; Pink J.R.; Davies G.; Kensil C.R.; Jeannin P.; Aubry J.-P.; Goetsch L.; Delneste Y.; Bonnefoy J.-Y.; Revets H.; De Baetselier P.; Steward M.; Fritchley S.J.; Bright J.R.; Oldroyd R.G.; Affleck L.J.; Ross T.M.; Holder A.A.; Smith R.A.G.; Kenney R.; Glenn G.; Czerkinsky C.; Del Giudice G.; Zurbriggen R.; Gluck R.; Drane D.; Pearse M.; Gander B.; Corradin G.; O'Hagan D.T.; Stewart V.A.; McGrath S.M.; Manganello L.; Davis S.A.; Kester K.E.; Cohen J.; Voss G.; Heppner D.G.; Pichyangkul S.; Miller R.S.; Tongtawe P.; Gettayacamin M.; Colgin L.; Rubel D.; Lyon J.; Angov E.; Ockenhouse C.F.; Ballou W.R.; Diggs C.L.; Walsh D.S.; Ahmad G.; Sachdeva S.; Bhardwaj A.; Lalitha P.V.; Rao P.P.; Chauhan V.S.; Long C.A.; Stowers A.; Wang J.; Lambert L.; Muratova O.; Saul A.; Miller L.; Pan W.; Huang D.; Zhang Q.; Qu L.; Zhang D.; Zhang X.; Qian F.; Handunnetti S.; Amaratunga C.; Perera L.; Weerasinghe S.; Rajakaruna J.; Perera K.; Gamage K.; Manamperi A.; Holm I.; Mendis K.; Longacre S.; Gosnell W.; Kramer K.J.; Hashimoto A.; Nishimura T.; Vine B.; Chang S.; Ganne V.; Van Nest G.; Perlaza B.L.; Hurtado S.; Gustavo Q.; Arevalo-Herrera M.; Druilhe P.Pierre; Herrera S.; Doolan D.L.; Sedegah M.; et al.
CORPORATE SOURCE: M.P. Kieny, World Health Organization/IVR, Avenue Appia 20, CH-1211, Geneva 27, Switzerland. Kienym@who.int
SOURCE: Vaccine, (2003) 21/25-26 (3503-3524).
ISSN: 0264-410X CODEN: VACCDE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English

L72 ANSWER 38 OF 64 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2003144925 EMBASE
TITLE: Novel generations of influenza vaccines.
AUTHOR: Kemble G.; Greenberg H.
CORPORATE SOURCE: G. Kemble, MedImmune Vaccines, 297 North Bernardo Avenue, Mountain View, CA 94043, United States.
kembleg@medimmune.com
SOURCE: Vaccine, (1 May 2003) 21/16 (1789-1795).
Refs: 59
ISSN: 0264-410X CODEN: VACCDE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Several strategies are being pursued to increase the quality and quantity of influenza vaccines that are used on an annual basis including increasing the immunogenicity of currently licensed inactivated vaccines, delivery of inactive vaccines directly to the nasal mucosa, the use of cell lines for virus production and the use of live, attenuated vaccines. In addition, modern molecular biological techniques are being used to create and evaluate new vaccine approaches. This report will briefly review these different strategies and outline some of the potential advantages and challenges associated with them.

L72 ANSWER 39 OF 64 EMBASE
on STN
ACCESSION NUMBER: 2003220506 EMBASE
TITLE: Recent advances in veterinary vaccine adjuvants.
AUTHOR: Singh M.; O'Hagan D.T.
CORPORATE SOURCE: M. Singh, Chiron Vaccines Research, Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608, United States. manmohan_singh@chiron.com
SOURCE: International Journal for Parasitology, (2003) 33/5-6 (469-478).
Refs: 110
ISSN: 0020-7519 CODEN: IJPYBT
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Next generation veterinary vaccines are going to mainly comprise of either subunit or inactivated bacteria/viruses. These vaccines would require optimal adjuvants and delivery systems to accord long-term protection from infectious diseases in animals. There is an urgent need for the development of new and improved veterinary and human vaccine adjuvants. Adjuvants can be broadly divided into two classes, based on their principal mechanisms of action: vaccine delivery systems and 'immunostimulatory adjuvants'. Vaccine delivery systems are generally particulate e.g. emulsions, microparticles, ISCOMS and liposomes, and mainly function to target associated antigens into antigen presenting cells (APC). In contrast, immunostimulatory adjuvants are predominantly derived from pathogens and often represent pathogen associated molecular patterns, e.g. LPS, MPL and CpG DNA, which activate cells of the innate immune system. Recent progress in innate immunity is beginning to yield insight into the initiation of immune responses and the ways in which immunostimulatory adjuvants might enhance this process in animals and humans alike.

L72 ANSWER 40 OF 64 EMBASE

on STN
ACCESSION NUMBER: 2003429063 EMBASE
TITLE: Immunostimulatory Oligonucleotides: Ready for Immunotherapy Prime Time!.
AUTHOR: Tam Y.K.
CORPORATE SOURCE: Dr. Y.K. Tam, Inex Pharmaceuticals Corporation, Burnaby, BC V5J 5J8, Canada. ytam@inexpharm.com
SOURCE: Journal of Hematotherapy and Stem Cell Research, (2003) 12/5 (467-471).
Refs: 16
ISSN: 1525-8165 CODEN: JHERFM
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
036 Health Policy, Economics and Management
037 Drug Literature Index
LANGUAGE: English

L72 ANSWER 41 OF 64 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
on STN
ACCESSION NUMBER: 2003232957 EMBASE
TITLE: Vaccines for Alzheimer's disease: How close are we?.
AUTHOR: Janus C.
CORPORATE SOURCE: Dr. C. Janus, Ctr. for Res. in Neurodeg. Diseases, University of Toronto, Tanz Neuroscience Building, 6 Queen's Park Crescent West, Toronto, Ont. M5S 3H2, Canada. janus@psych.utoronto.ca
SOURCE: CNS Drugs, (2003) 17/7 (457-474).
Refs: 113
ISSN: 1172-7047 CODEN: CNDREF
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 008 Neurology and Neurosurgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Alzheimer's disease is a neurodegenerative disorder characterised by a progressive loss of cognitive function. Despite the considerable progress being made, a complete description of the molecular pathology of this disease has yet to be elucidated. The evidence indicates that abnormal processing and extracellular deposition of the longer form of the β-amyloid (Aβ) peptide (Aβ(1-42), a proteolytic derivative of the amyloid precursor protein [APP]) is implicated in the pathogenesis of Alzheimer's disease. In this respect, recent use of experimental mouse models, in which the mice develop some aspects of Alzheimer's disease in a reproducible fashion, has provided a new opportunity for a multidisciplinary and invasive analysis of mechanisms behind the amyloid pathology and its role in Alzheimer's disease. It has been demonstrated, using a single transgenic mouse model system that overexpresses the human mutated APP gene, that an immunisation against Aβ(1-42) causes a marked reduction in the amyloid burden in the brain. The follow-up research provided more evidence that both active and passive Aβ immunisation also reduces cognitive dysfunction in transgenic mouse models of Alzheimer's disease. Other studies using different approaches - such as secretase, cholesterol and Aβ metalloprotein inhibitors or NSAIDs - but all targeting the abnormal metabolism of Aβ have confirmed in each case that a significant reduction of amyloid plaque burden can be achieved in transgenic mouse models of Alzheimer's disease. This research

strongly supports the notion that abnormal Aβ processing is essential to the pathogenesis of Alzheimer's disease and provides a crucial platform for the development and detailed testing of potential treatments in experimental models before each of these approaches can be proposed as a therapy for Alzheimer's disease. Although the first clinical trial of active immunisation with a pre-aggregated synthetic Aβ(42) preparation (AN-1792 vaccine) met with some setbacks and was discontinued after several patients experienced meningoencephalitis, the follow-up analysis of the effect of immunisation against Aβ in humans revealed a powerful effect of vaccination in the clearance of amyloid plaques from the cerebral cortex.

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ACCESSION NUMBER: 2003192790 EMBASE
TITLE: Microparticles as vaccine adjuvants and delivery systems.
AUTHOR: O'Hogan D.T.; Singh M.
CORPORATE SOURCE: Dr. D.T. O'Hogan, Vaccine Research, Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608, United States. derek_o'hagan@chiron.com
SOURCE: Expert Review of Vaccines, (2003) 2/2 (269-283). Refs: 169 ISSN: 1476-0584 CODEN: ERVXAX
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Adjuvants can be broadly divided into two groups, based on their principal mechanisms of action: vaccine delivery systems and immunostimulatory adjuvants. Vaccine delivery systems are generally particulate (e.g., emulsions, microparticles, immunostimulatory complexes and liposomes) and function mainly to target associated antigens into antigen-presenting cells. However, increasingly, more complex formulations are being developed in which delivery systems are exploited both for the delivery of antigens and also for the delivery of coadministered immunostimulatory adjuvants. The rationale for this approach is to ensure that both antigen and adjuvant are delivered into the same population of antigen-presenting cells. In addition, delivery systems can focus the effect of the adjuvants onto the key cells of the immune system and limit the systemic distribution of the adjuvant, to minimize its potential to Induce adverse effects. The formulation and delivery of potent adjuvants in microparticles may allow the development of prophylactic and therapeutic vaccines against cancers and chronic Infectious diseases, which are currently poorly controlled. In addition, microparticle formulations may also allow vaccines to be delivered mucosally.

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ACCESSION NUMBER: 2003176966 EMBASE
TITLE: The 8(th) International Conference on Alzheimer's Disease and Related Disorders, July 20-25, 2002, Stockholm, Sweden.
AUTHOR: Kimberly W.T.; Kovacs D.M.; Walsh D.; Lashuel H.; Lemere C.A.
CORPORATE SOURCE: Dr. C.A. Lemere, Center for Neurologic Diseases, Harvard Institutes of Medicine, 77 Avenue Louis Pasteur, Boston, MA 02115, United States. lemere@cnd.bwh.harvard.edu
SOURCE: Amyloid, (2003) 10/1 (51-61).

ISSN: 1350-6129 CODEN: AIJIET
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 008 Neurology and Neurosurgery
017 Public Health, Social Medicine and Epidemiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L72 ANSWER 44 OF 64 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003031001 EMBASE
TITLE: The biological action of saponins in animal systems: A review.
AUTHOR: Francis G.; Kerem Z.; Makkar H.P.S.; Becker K.
CORPORATE SOURCE: Prof. Dr. K. Becker, Dept. of Aquacul. Syst./Anim. Nutr., Inst. for Anim. Prod. in the Tropics, University of Hohenheim (480), D 70593 Stuttgart, Germany. kbecker@uni-hohenheim.de
SOURCE: British Journal of Nutrition, (1 Dec 2002) 88/6 (587-605). Refs: 214
ISSN: 0007-1145 CODEN: BJNUAV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
029 Clinical Biochemistry
018 Cardiovascular Diseases and Cardiovascular Surgery
004 Microbiology
048 Gastroenterology
008 Neurology and Neurosurgery
052 Toxicology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Saponins are steroid or triterpenoid glycosides, common in a large number of plants and plant products that are important in human and animal nutrition. Several biological effects have been ascribed to saponins. Extensive research has been carried out into the membrane-permeabilising, immunostimulant, hypocholesterolaemic and anticarcinogenic properties of saponins and they have also been found to significantly affect growth, feed intake and reproduction in animals. These structurally diverse compounds have also been observed to kill protozoans and molluscs, to be antioxidants, to impair the digestion of protein and the uptake of vitamins and minerals in the gut, to cause hypoglycaemia, and to act as antifungal and antiviral agents. These compounds can thus affect animals in a host of different ways both positive and negative.

L72 ANSWER 45 OF 64 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001275310 EMBASE
TITLE: Towards the rational design of Th1 adjuvants.
AUTHOR: Moingeon P.; Haensler J.; Lindberg A.
CORPORATE SOURCE: P. Moingeon, Department of Research/Development, Campus Merieux, 1541 avenue Marcel Merieux, 69280 Marcy l'Etoile, France. philippe.moingeon@aventis.com
SOURCE: Vaccine, (14 Aug 2001) 19/31 (4363-4372). Refs: 97
ISSN: 0264-410X CODEN: VACCDE
PUBLISHER IDENT.: S 0264-410X(01)00193-1

COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Finding adjuvants in order to enhance immune responses against target immunogens has been a major and recurrent issue for the vaccine industry. It is yet to be solved, most particularly in the context of a growing interest in designing new types of vaccines capable of eliciting Th1 immune responses. A review of synthetic adjuvants which have been (or are being) tested in clinical studies is presented. Importantly, recent advances in our understanding of the physiology of immune responses offer new avenues to design and test candidate adjuvants, based on either synthetic or natural molecules, with the aim to mimic and recapitulate pro-inflammatory signals initiating both innate and adaptative immune effector mechanisms. Thus, adjuvants of the future might be a mixture of molecules selected singularly for a capacity to attract, target or activate professional antigen presenting cells. Used as a combination, such molecules should facilitate antigen presentation by professional APCs and lead to a potent induction of T cell-mediated effector and immune memory mechanisms. .COPYRGT. 2001 Published by Elsevier Science Ltd.

L72 ANSWER 46 OF 64 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2001428655 EMBASE
TITLE: Immunological adjuvants in allergy vaccines: Past, present and future.
AUTHOR: Wheeler A.W.; Woroniecki S.R.
CORPORATE SOURCE: Dr. A.W. Wheeler, Allergy Therapeutics Ltd., Dominion Way, Worthing, West Sussex BN14 8SA, United Kingdom. Alan.Wheeler@Allergytherapeutics.com
SOURCE: Allergology International, (2001) 50/4 (295-301).
Refs: 50
ISSN: 1323-8930 CODEN: ALINFR
COUNTRY: Australia
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hundreds of compounds have been tested over the years in a search for adjuvants to incorporate with antigens or allergens to enhance the immune response. Despite this, aluminum salts have been the only adjuvants that have been both registered for clinical application and used on a large scale until recently. Salts of aluminum, such as aluminum hydroxide, have been used as general immunologic adjuvants for several decades. Some allergen vaccines used for the treatment of allergy are still formulated with aluminum-based adjuvants. These formulations have generally proved efficacious and have a good safety profile compared with simple aqueous extracts. However, there is reported sensitivity and toxicity associated with use of aluminum. In addition, aluminum salts are known to be potent stimulators of T helper (h) 2 cell activity. Because Th2 activity directs towards an allergic response, aluminum salts are potentially counterproductive when used as adjuvants in the immunologic treatment of type 1 hypersensitivity. Many soluble and insoluble molecules have been reported to have adjuvant activity in experimental systems. Some of these

have been used clinically, but side effects, such as local granuloma formation, have led to their withdrawal from clinical use. Newer depottype adjuvants, such as insoluble calcium salts, tyrosine (now registered) and coupled alginates, may eliminate some of the potential problems of aluminum salts and are currently used in some allergy vaccines but have not as yet formed a complete replacement. Liposomes, iscoms and biodegradable microspheres are now being considered for clinical use as adjuvants for both oral and parenteral routes. Soluble adjuvants that are capable of directing the immune response in a more selective way are currently in development for use in allergy vaccines. One of these, the Th1-directing adjuvant monophosphoryl lipid A (MPL(®); Corixa, Seattle, WA, USA), is now in clinical use in allergy vaccines formulated with the depot adjuvant L-tyrosine. Other ways of stimulating a Th1 response using immunostimulatory DNA sequences (immunostimulatory DNA sequences (ISS) or CpG motifs) as 'built-in' adjuvants are being studied. Further interesting adjuvants reported in the literature, such as Montanide ISA 720, SAF-m, RC-529 and QS21, may also be applicable to allergy vaccination.

L72 ANSWER 47 OF 64 EMBASE
on STN

ACCESSION NUMBER: 2001335337 EMBASE
TITLE: Recent developments in adjuvants for vaccines against infectious diseases.
AUTHOR: O'Hagan D.T.; MacKichan M.L.; Singh M.
CORPORATE SOURCE: D.T. O'Hagan, Chiron Corporation, Immunology and Infectious Diseases, 4560 Horton Street, Emeryville, CA 94608, United States. derek_o'hagan@chiron.com
SOURCE: Biomolecular Engineering, (2001) 18/3 (69-85).
Refs: 220
ISSN: 1389-0344 CODEN: BIENFV
PUBLISHER IDENT.: S 1389-0344(01)00101-0
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB New generation vaccines, particularly those based on recombinant proteins and DNA, are likely to be less reactogenic than traditional vaccines, but are also less immunogenic. Therefore, there is an urgent need for the development of new and improved vaccine adjuvants. Adjuvants can be broadly separated into two classes, based on their principal mechanisms of action; vaccine delivery systems and 'immunostimulatory adjuvants'. Vaccine delivery systems are generally particulate e.g. emulsions, microparticles, iscoms and liposomes, and mainly function to target associated antigens into antigen presenting cells (APC). In contrast, immunostimulatory adjuvants are predominantly derived from pathogens and often represent pathogen associated molecular patterns (PAMP) e.g. LPS, MPL, CpG DNA, which activate cells of the innate immune system. Once activated, cells of innate immunity drive and focus the acquired immune response. In some studies, delivery systems and immunostimulatory agents have been combined to prepare adjuvant delivery systems, which are designed for more effective delivery of the immunostimulatory adjuvant into APC. Recent progress in innate immunity is beginning to yield insight into the initiation of immune responses and the ways in which immunostimulatory adjuvants may enhance this process. However, a rational

approach to the development of new and more effective vaccine adjuvants will require much further work to better define the mechanisms of action of existing adjuvants. The discovery of more potent adjuvants may allow the development of vaccines against infectious agents such as HIV which do not naturally elicit protective immunity. New adjuvants may also allow vaccines to be delivered mucosally. .COPYRGT. 2001 Published by Elsevier Science B.V.

L72 ANSWER 48 OF 64 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000082435 EMBASE
TITLE: Vaccines adjuvants.
AUTHOR: Newman M.J.
CORPORATE SOURCE: M.J. Newman, Infectious Disease Program, Epimmune, Inc., 5820 Nancy Ridge Drive, San Diego, CA 92121, United States. mnewman@epimmune.com
SOURCE: Expert Opinion on Therapeutic Patents, (2000) 10/3 (297-314).
Refs: 273
ISSN: 1354-3776 CODEN: EOTPEG
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB A wide variety of adjuvant-active materials have been used in experimental and veterinary vaccines but the only commonly used adjuvants for human vaccines are based on aluminium salts. The reasons for this are numerous but most new adjuvant products have failed in the developmental stage due to toxicity or limitations associated with manufacturing and stability. Research completed over the last 30 years is now providing products with significant potential for improving the efficacy of human vaccines. These new products are derived from many different sources, including natural products, such as plant saponins, bacterial lipopolysaccharides, biodegradable oils and lipids, and novel synthetic polymers. Individual adjuvants exert varied effects on the immune system and many products can be used in combination formulations. This degree of flexibility will allow for vaccines to be optimally formulated for specific disease targets. The ability to produce more potent vaccines, through the use of adjuvants, is critical to the expansion of this field, especially for vaccines targeting pathogens where no form of protection exists. Examples of pathogen targets used most commonly to clinically evaluate new adjuvant technologies include HIV-1 and the causative agent of human malaria, Plasmodium falciparum. Adjuvants may also provide significant benefit to those segments of the population that are partially immunocompromised, such as the elderly. Finally, highly potent adjuvant-supplemented vaccines have shown promise as therapeutics for the treatment of cancer; products that can be used to supplement established therapies. Descriptions of the advantages and limitations of adjuvants that are most likely to be available for use as components in licensed vaccines within the next decade have been included in this review.

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ACCESSION NUMBER: 2000094262 EMBASE
TITLE: Delivery systems for molecular vaccination.
AUTHOR: Sheikh N.A.; Al-Shamisi M.; Morrow W.J.W.

CORPORATE SOURCE: N.A. Sheikh, Department of Pharmaceutics, Washington Reg. Primate Res. Center, University of Washington, Seattle, WA 98121, United States
SOURCE: Current Opinion in Molecular Therapeutics, (2000) 2/1 (37-54).
Refs: 162
ISSN: 1464-8431 CODEN: CUOTFO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Vaccination is one of the medical success stories of the 20th century, however, there are many diseases for which no prophylactic regimes are available. A major hindrance that has prevented the development of effective mass immunization programs is the inability to induce an appropriate, protective, immune response. For example, for vaccines against intracellular pathogens there is a requirement for cell-mediated immunity as characterized by cytolytic T-lymphocyte activity. However, such a response can be extremely difficult to elicit, especially those employing recombinant, soluble protein subunits. This deficiency is due to the inability of these antigens to access the machinery of the appropriate antigen-processing pathway. Following an improved understanding of the mechanisms underlying such processing, as well as the realization that delivery systems can affect, quantitatively and qualitatively, the resulting immune response, the last decade has witnessed an intense research effort in this field. In this article we will review the major developments in the area of antigen delivery as related to vaccination.

L72 ANSWER 50 OF 64 EMBASE
on STN
ACCESSION NUMBER: 1999203505 EMBASE
TITLE: Novel adjuvants currently in clinical testing November 2-4, 1998, Fondation Merieux, Annecy, France: A meeting sponsored by the World Health Organization.
AUTHOR: Aguado T.; Engers H.; Pang T.; Pink R.
CORPORATE SOURCE: H. Engers, World Health Organization, CH-1211 Geneva 27, Switzerland
SOURCE: Vaccine, (14 May 1999) 17/19 (2321-2328).
Refs: 15
ISSN: 0264-410X CODEN: VACCDE
PUBLISHER IDENT.: S 0264-410X(99)00021-3
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L72 ANSWER 51 OF 64 EMBASE
on STN
ACCESSION NUMBER: 1999396555 EMBASE
TITLE: Advances in vaccine adjuvants.
AUTHOR: Singh M.; O'Hagan D.
CORPORATE SOURCE: M. Singh, Chiron Corporation, 5300 Chiron Way, Emeryville, CA 94608, United States
SOURCE: Nature Biotechnology, (1999) 17/11 (1075-1081).

Refs: 120
ISSN: 1087-0156 CODEN: NABIF
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Currently, aluminum salts and MF59 are the only vaccine adjuvants approved for human use. With the development of new-generation vaccines (including recombinant subunit and mucosal vaccines) that are less immunogenic, the search for more potent vaccine adjuvants has intensified. Of the novel compounds recently evaluated in human trials, immunostimulatory molecules such as the lipopolysaccharide derived MPL and the saponin derivative QS21 appear most promising, although doubts have been raised as to their safety in humans. Preclinical work with particulate adjuvants, such as the MF59 microemulsion and lipid-particle immune-stimulating complexes (Iscoms), suggest that these molecules are also potent elicitors of humoral and cellular immune responses. In addition, preclinical data on CpG oligonucleotides appear to be encouraging, particularly with respect to their ability to selectively manipulate immune responses. While all these adjuvants show promise, further work is needed to better define the mechanisms of adjuvant action. Ultimately, the development of more potent adjuvants may allow vaccines to be used as therapeutic, rather than prophylactic, agents.

L72 ANSWER 52 OF 64 EMBASE
on STN

ACCESSION NUMBER: 1998414931 EMBASE
TITLE: ISCOMs: An adjuvant with multiple functions.
AUTHOR: Sjolander A.; Cox J.C.; Barr I.G.
CORPORATE SOURCE: A. Sjolander, Immunology Department, CSL Limited, 45 Poplar Road, Melbourne, Vic. 3052, Australia. asjoland@csl.com.au
SOURCE: Journal of Leukocyte Biology, (1998) 64/6 (713-723).
Refs: 152
ISSN: 0741-5400 CODEN: JLBIE7
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Aluminum salts are currently the only widely used adjuvant for human vaccines. Over the past 10-15 years, a large research effort has attempted to find novel adjuvants with ability to induce a broad range of immune responses, including cell-mediated immunity. The immunostimulating complex or ISCOM is one adjuvant with multiple adjuvant properties. ISCOMs are open cage-like complexes typically with a diameter of about 40 nm that are built up by cholesterol, lipid, immunogen, and saponins from the bark of the tree Quillaia saponaria Molina. ISCOMs have been demonstrated to promote antibody responses and induce T helper cell as well as cytotoxic T lymphocyte responses in a variety of experimental animal models, and have now progressed to phase I and II human trials. This review describes recent developments in the understanding of the structure, composition, and preparation of ISCOMs and will cover important aspects of the understanding of the adjuvant functions of ISCOMs and how they act on the immune system.

L72 ANSWER 53 OF 64 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1998125325 EMBASE
TITLE: Preservation of mucosal and systemic adjuvant properties of ISCOMS in the absence of functional interleukin-4 or interferon-γ.
AUTHOR: Smith R.E.; Donachie A.M.; McLaren F.H.; Mowat A.M.
CORPORATE SOURCE: Dr. R.E. Smith, Department of Immunology, University of Glasgow, Western Infirmary, Glasgow G11 6NT, United Kingdom
SOURCE: Immunology, (1998) 93/4 (556-562).
Refs: 47
ISSN: 0019-2805 CODEN: IMMUAM
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Adjuvants are a critical component of non-viable vaccine vectors, particularly for those to be used via mucosal routes. Although most adjuvants act by inducing local inflammatory responses, the molecular basis of many of these effects is unclear. Here we have investigated whether interleukin-4 (IL-4) and interferon-γ (IFN-γ) are required for the induction of local and systemic immune responses by oral and parenteral administration of ovalbumin (OVA) in immune stimulating complexes (ISCOMS), a potent mucosal adjuvant vector. Our results show that after oral or systemic immunization with OVA ISCOMS, IL-4 knockout (IL4KO) and IFN-γ receptor knockout (IFN-γRKO) mice develop an entirely normal range of immune responses including delayed-type hypersensitivity (DTH), serum immunoglobulin G (IgG) antibodies, T-cell proliferation and cytokine production, class I major histocompatibility complex (MHC)-restricted cytotoxic T lymphocyte (CTL) activity and intestinal IgA antibodies. These responses were of a similar magnitude to those found in the wild-type mice, indicating that the immunogenicity of ISCOMS is not influenced by the presence of IL-4 or IFN-γ and emphasizing the potential of ISCOMS as widely applicable mucosal adjuvants.

L72 ANSWER 54 OF 64 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 1999016458 EMBASE
TITLE: Approaches to new vaccines.
AUTHOR: Mahon B.P.; Moore A.; Johnson P.A.; Mills K.H.G.
CORPORATE SOURCE: B.P. Mahon, Infection and Immunity Group, National University of Ireland, Maynooth, County Kildare, Ireland
SOURCE: Critical Reviews in Biotechnology, (1998) 18/4 (257-282).
Refs: 161
ISSN: 0738-8551 CODEN: CRBTE5
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
027 Biophysics, Bioengineering and Medical Instrumentation
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The explosive technological advances in the fields of immunology and

molecular biology in the last 5 years had an enormous impact on the identification of candidate vaccines against diseases, which until a few years ago seemed uncontrollable. Increased knowledge of the immune system has helped to define the mechanisms that underlie successful immunization and is now being exploited to develop improved versions of existing vaccines and new vaccines against emerging pathogens, tumors, or autoimmune diseases. An understanding of the mechanisms of action of novel adjuvants and the development of new vector and delivery systems will have a major impact on vaccine strategies. The use of DNA encoding antigens from pathogenic viruses, bacteria, and parasites as vaccines is a new approach that is receiving considerable attention. This and other innovative approaches, including vaccine production in plants, are appraised in this review. The successful eradication of smallpox and the imminent eradication of poliomyelitis by worldwide immunization campaigns provide positive examples of how the vaccine-mediated approach can lead to disease elimination; with the advent of new vaccines and improved delivery systems, there is no scientific reason why these successes cannot be repeated.

L72 ANSWER 55 OF 64 EMBASE
on STN

ACCESSION NUMBER: 95321063 EMBASE
DOCUMENT NUMBER: 1995321063
TITLE: Adjuvants for human vaccines. Current status, problems and future prospects.
AUTHOR: Gupta R.K.; Siber G.R.
CORPORATE SOURCE: MA Public Health Biologic Labs., State Laboratory Institute,Boston, MA 02130, United States
SOURCE: Vaccine, (1995) 13/14 (1263-1276).
ISSN: 0264-410X CODEN: VACCDE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Adjuvants help antigen to elicit an early, high and long-lasting immune response with less antigen, thus saving on vaccine production, costs. In recent years, adjuvants received much attention because of the development of purified, subunit and synthetic vaccines which are poor immunogens and require adjuvants to evoke the immune response. With the use of adjuvants immune response can be selectively modulated to major histocompatibility complex (MHC) class I or MHC class II and Th1 or Th2 type, which is very important for protection against diseases caused by intracellular pathogens such as viruses, parasites and bacteria (Mycobacterium). A number of problems are encountered in the development and use of adjuvants for human vaccines. The biggest issue with the use of adjuvants for human vaccines, particularly routine childhood vaccines is the toxicity and adverse side-effects of most of the adjuvant formulations. At present the choice of adjuvants for human vaccination reflects a compromise between a requirement for adjuvanticity and an acceptable low level of side-effects. Other problems with the development of adjuvants include restricted adjuvanticity of certain formulations to a few antigens, use of aluminum adjuvants as reference adjuvant preparations under suboptimal conditions, non-availability of reliable animal models, use of non-standard assays and biological differences between animal models and humans leading to the failure of promising formulations to show adjuvanticity in clinical trials. The most common adjuvants for human use today are still aluminum hydroxide and aluminum phosphate, although calcium phosphate and oil

emulsions also have some use in human vaccinations. During the last 15 years much progress has been made on development, isolation and chemical synthesis of alternative adjuvants such as derivatives of muramyl dipeptide, monophosphoryl lipid A, liposomes, QS21, MF-59 and immunostimulating complexes (ISCOMS). Other areas in adjuvant research which have received much attention are the controlled release of vaccine antigens using biodegradable polymer microspheres and reciprocal enhanced immunogenicity of protein-polysaccharide conjugates. Biodegradable polymer microspheres are being evaluated for targeting antigens on mucosal surfaces and for controlled release of vaccines with an aim to reduce the number of doses required for primary immunization. Reciprocal enhanced immunogenicity of protein-polysaccharide conjugates will be useful for the development of combination vaccines.

L72 ANSWER 56 OF 64 EMBASE
on STN

ACCESSION NUMBER: 95159377 EMBASE
DOCUMENT NUMBER: 1995159377
TITLE: Immunostimulating complexes. Clinical potential in vaccine development.
AUTHOR: Morein B.; Lovgren K.; Ronnberg B.; Sjolander A.; Villacres-Eriksson M.
CORPORATE SOURCE: Swedish Univ. of Agricultural Scis., Faculty of Veterinary Medicine, Biomedical Centre, Box 585,S-751 23 Uppsala, Sweden
SOURCE: Clinical Immunotherapeutics, (1995) 3/6 (461-475). ISSN: 1172-7039 CODEN: CIMMEA
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB An immunostimulating complex (iscom) is a particle containing several copies of an antigen, with a built-in adjuvant. It is constructed to provide a physically optimal presentation of antigen to the immune system. An iscom particle without incorporated antigen is called the iscom matrix, or just matrix, and can be used as a conventional adjuvant that is added to the antigen whose immunogenicity is to be reinforced. The unique components of the iscom matrix are saponins (triterpenoids) from the tree **Quillaja** saponaria, which exhibit a unique affinity for cholesterol and thereby facilitate the stability of the complex. The triterpenoids can be used as a crude preparation of **Quillaja** saponins or as purified preparations of **Quillaja** triterpenoids. The various triterpenoids have different characteristics, of which some are relevant to vaccine development such as the iscom-forming capacity, the immunomodulatory capacity, a low cell lytic property and low toxicity in general. Consequently, various compositions of triterpenoids, including efficient nontoxic adjuvant formulations or inert carrier formulations, can be made. The currently used iscom vaccine and experimental vaccines induce a broad immune response, including major histocompatibility complex (MHC) class I and II T cell responses. The MHC class II response encompasses a prominent response of T helper 1 (T(H)1)-like cells, producing interleukin (IL)-2 and interferon-γ and favouring cell-mediated immunity. A T(H)2-like response may also be evoked, with cells producing IL-4 and IL-10 and promoting humoral immunity. However, the same influenza virus envelope antigen in a micellar nonadjuvanted torm induces a more prominent T(H)2 type of response, with cells producing more

IL-10. The iscom particle is also an interesting nonreplicating candidate for induction of mucosal immunity. Iscoms containing different kinds of antigens in various experimental vaccines evoke secretory IgA or cytotoxic T cell responses when administered orally and intranasally. Experimental iscom vaccine formulations have been shown to induce protective immunity to a number of micro-organisms, including viruses and retroviruses, parasites and bacteria, in several species, including primates.

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ACCESSION NUMBER: 74117545 EMBASE
DOCUMENT NUMBER: 1974117545
TITLE: Preparation of inactivated vaccines against alpha viruses using semliki forest virus: white mouse as a model. I. Inactivation experiments and evaluation of double inactivated subunit vaccines.
AUTHOR: Mussgay M.; Weiland E.
CORPORATE SOURCE: Fed. Res. Inst. Anim. Virus Dis., Tubingen, Germany
SOURCE: Intervirology, (1973) 1/4 (259-268).
CODEN: IVRYAK
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
047 Virology
LANGUAGE: English

AB Inactivation of Semliki Forest virus (SFV) with formalin, β propiolactone, hydroxylamine and 2 ethylethylenimine was studied. Immunogenicity of SFV was best retained after formalin inactivation. Vaccines were prepared by applying two inactivation procedures in the following order: (a) disruption of SFV by either Tween 80 ether, NP 40 or deoxycholate, or treatment of SFV with saponin; (b) addition of either formalin, β propiolactone, hydroxylamine or 2 ethylethylenimine. These vaccines were evaluated in white mice, in several experiments. It was concluded that a gradient from potent to less or non potent vaccines exists in the order saponin formalin, Tween 80 ether formalin and NP 40 ethylethylenimine or deoxycholate formalin inactivation, but none of these vaccines was superior to reference vaccines containing only formalin inactivated virus.

L72 ANSWER 58 OF 64 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2003:97931 BIOSIS
DOCUMENT NUMBER: PREV200300097931
TITLE: **Vaccine** comprising an iscom consisting of **sterol** and **saponin** which is free of additional **detergent**.
AUTHOR(S): Friede, Martin [Inventor, Reprint Author]; Garcon, Nathalie Marie-Josephe Claude [Inventor]
CORPORATE SOURCE: Farnham, UK
ASSIGNEE: SmithKline Beecham Biologicals, S.A., Rixensart, Belgium
PATENT INFORMATION: US 6506386 January 14, 2003
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Jan 14 2003) Vol. 1266, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print).
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Feb 2003
Last Updated on STN: 12 Feb 2003

AB The present invention provides an improved adjuvant formulation and a process for producing said adjuvant. The adjuvant comprises an ISCOM

structure comprising a **saponin**, said ISCOM structure being devoid of additional detergent.

L72 ANSWER 59 OF 64 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2004:22495 BIOSIS
DOCUMENT NUMBER: PREV200400009867
TITLE: Effectiveness of the **quillaja** saponin semi-synthetic **analog** GPI-0100 in potentiating mucosal and systemic responses to recombinant HagB from Porphyromonas gingivalis.
AUTHOR(S): Zhang, Ping; Yang, Qiu-Bo; Marciani, Dante J.; Martin, Michael; Clements, John D.; Michalek, Suzanne M.; Katz, Jannet [Reprint Author]
CORPORATE SOURCE: Department of Oral Biology, University of Alabama at Birmingham, 845 19th Street South, BBRB 258/5, Birmingham, AL, 35294-2170, USA
jenny_kataz@micro.microbio.uab.edu
SOURCE: Vaccine, (1 October 2003) Vol. 21, No. 27-30, pp. 4459-4471. print.
ISSN: 0264-410X (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Dec 2003
Last Updated on STN: 24 Dec 2003

AB The gram-negative, anaerobic bacterium Porphyromonas gingivalis, has been implicated in the etiology of adult periodontal disease. Among the potential virulence factors of this bacterium, the non-fimbrial adhesin hemagglutinin B (HagB) appears to be involved in the initial adherence of the bacteria to host tissue and the induction of anti-HagB antibody responses affords some protection from experimental alveolar bone loss. In the present study, we have investigated the ability of the **quillaja** saponin derivative GPI-0100 to act as an immunostimulant of responses to HagB following subcutaneous (s.c.) or intranasal (i.n.) immunization of mice. We have also compared the immunopotentiating ability of GPI-0100 with that of five other adjuvants. Evidence is provided that GPI-0100 was more effective than monophosphoryl **lipid** A and alum in inducing serum anti-HagB responses following s.c. immunization. A comparison of the responses induced following i.n. immunization with HagB and adjuvant revealed that the heat-labile toxin of Escherichia coli (LT) and the non-enzymatic mutant LT (E112K), followed by GPI-0100 potentiated higher serum and mucosal anti-HagB antibody responses, which in most cases were higher than those seen with the other adjuvants tested (i.e. monophosphoryl **lipid** A, alum and the B subunit of cholera toxin). Furthermore, a difference was seen in the nature of the serum IgG anti-HagB response based on the adjuvant used and route of immunization. These results demonstrate the effectiveness of GPI-0100 as both a systemic and mucosal adjuvant and support its potential use in the development of **vaccines** against periodontal, as well as other pathogens.

L72 ANSWER 60 OF 64 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2002:293867 BIOSIS
DOCUMENT NUMBER: PREV200200293867
TITLE: **Vaccines.**
AUTHOR(S): Garcon, Nathalie [Inventor, Reprint author]; Momin, Patricia Marie Christine Aline Francoise [Inventor]
CORPORATE SOURCE: Wavre, Belgium
ASSIGNEE: SmithKline Beecham Biologicals, s.a., Rixensart, Belgium
PATENT INFORMATION: US 6372227 April 16, 2002

SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Apr. 16, 2002) Vol. 1257, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 15 May 2002
Last Updated on STN: 15 May 2002

AB The present invention relates to **oil** in **water emulsion** compositions, their use in medicine, in particular to their use in augmenting immune responses to a wide range of antigens, and to methods of their manufacture; the compositions having oil phase and an aqueous phase, a **sterol** and a **saponin**; the **sterol** being present in the oil phase and the **saponin** being present in the aqueous phase.

L72 ANSWER 61 OF 64 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:122085 BIOSIS
DOCUMENT NUMBER: PREV200100122085
TITLE: Immunostimulating and **vaccine** compositions employing saponin **analog** adjuvants and uses thereof.
AUTHOR(S): Marciani, Dante J. [Inventor, Reprint author]
CORPORATE SOURCE: Brimingham, AL, USA
ASSIGNEE: Galenica Pharmaceuticals, Inc., Frederick, MD, USA
PATENT INFORMATION: US 6080725 June 27, 2000
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (June 27, 2000) Vol. 1235, No. 4. e-file. CODEN: OGUPE7. ISSN: 0098-1133.
DOCUMENT TYPE: Patent
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Mar 2001
Last Updated on STN: 15 Feb 2002

AB The present invention is directed to **vaccines** comprising (1) one or more bacterial, viral or tumor-associated antigens; and (2) one or more saponin-lipophile conjugate in which a lipophilic moiety such as a **lipid**, fatty acid, polyethylene glycol or terpene is covalently attached to a non-acylated or desacylated triterpene saponin via a carboxyl group present on the 3-O-glucuronic acid of the triterpene saponin. The attachment of a lipophile moiety to the 3-O-glucuronic acid of a saponin such as **Quillaja** desacylsaponin, lucyoside P, or saponin from Gypsophila, Saponaria and Acanthophyllum enhances their adjuvant effects on humoral and cell mediated immunity. Additionally, the attachment of a lipophile moiety to the 3-O-glucuronic acid residue of non- or des-acylsaponin yields a saponin analog that is easier to purify, less toxic, chemically more stable, and possesses equal or better adjuvant properties than the original saponin.

L72 ANSWER 62 OF 64 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1996:81762 BIOSIS
DOCUMENT NUMBER: PREV199698653897
TITLE: Experimental anthrax **vaccines**: Efficacy of adjuvants combined with protective antigen against an aerosol Bacillus anthracis spore challenge in **guinea** pigs.
AUTHOR(S): Ivins, Bruce; Fellows, Patricia; Pitt, Louise; Estep, James; Farchaus, Joseph; Friedlander, Arthur; Gibbs, Paul
CORPORATE SOURCE: Bacteriol. Div., United States Army Med. Res. Inst. Infectious Diseases, Fort Detrick, Frederick, MD

21702-5011, USA
SOURCE: Vaccine, (1995) Vol. 13, No. 18, pp. 1779-1784.
CODEN: VACCDE. ISSN: 0264-410X.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Feb 1996
Last Updated on STN: 10 Jun 1997

AB The efficacy of several human anthrax **vaccine** candidates comprised of different adjuvants together with Bacillus anthracis protective antigen (PA) was evaluated in guinea pigs challenged by an aerosol of virulent B. anthracis spores. The most efficacious **vaccines** tested were formulated with PA plus monophosphoryl **lipid** A (MPL) in a squalene/lecithin/Tween 80 emulsion (SLT) and PA plus the saponin **QS-21**. The PA+MPL in SLT **vaccine**, which was lyophilized and then reconstituted before use, demonstrated strong protective immunogenicity, even after storage for 2 years at 4 degree C. The MPL component was required for maximum efficacy of the **vaccine**. Eliminating lyophilization of the **vaccine** did not diminish its protective efficacy. No significant alteration in efficacy was observed when PA was dialyzed against different buffers before preparation of **vaccine**. PA +MPL in SLT proved superior in efficacy to the licensed United States human anthrax **vaccine** in the guinea pig model.

L72 ANSWER 63 OF 64 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1994:551104 BIOSIS
DOCUMENT NUMBER: PREV199598010652
TITLE: Systemic Cytokine Profiles in BALB/c Mice Immunized with Trivalent Influenza **Vaccine** Containing MF59 Oil **Emulsion** and Other Advanced Adjuvants.
AUTHOR(S): Valensi, Jean-Paul M.; Carlson, Julia R.; Van Nest, Gary A. [Reprint author]
CORPORATE SOURCE: Chiron Corp., 4560 Horton St., Emeryville, CA 94608, USA
SOURCE: Journal of Immunology, (1994) Vol. 153, No. 9, pp. 4029-4039.
CODEN: JOIMA3. ISSN: 0022-1767.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Dec 1994
Last Updated on STN: 23 Feb 1995

AB We have studied serum cytokine profiles in BALB/c mice after immunization with influenza **vaccine** alone or combined with the following adjuvants: alum; MF59 emulsion, MF59 containing the muramyl peptide N-acetyl-muramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1,2-dipalmitoyl-sn-glycero-3-(hydroxyphosphoryloxy))ethylamide (MTP-PE); MF59 plus the **lipid** A analogue monophosphoryl **lipid** A; MF59 plus the Quil A **saponin** fraction LTC; or LTC alone. Pooled mouse sera were analyzed by ELISA at various times after immunization for IL-1-alpha, IL-2, IL-3, IL-4, IL-5, IL-6, IL-10, IFN-gamma, and TNF-alpha. In naive mice, **vaccine** alone induced low levels of IL-3 and IL-5 only; **vaccine** plus alum induced a low IL-6 response as well. The MF59-based adjuvants significantly increased the IL-5 and IL-6 levels, whereas Quil A LTC induced strong IFN-gamma and measurable IL-2 responses, in addition to moderate IL-5 and IL-6. In previously infected mice, MF59 and MF59/MTP-PE were capable of generating IFN-gamma responses, as well as IL-5 and IL-6. All of the cytokine responses were rapid (peaking 3 to 12 h postimmunization) and short lived. In naive mice, the MF59 adjuvants induced serum cytokine profiles that are consistent with a primarily Th2-type response, whereas the Quil A LTC induced cytokines associated with both Th1 and Th2 responses. Ab analyses indicated that, although the

adjuvants strongly affected the magnitude of the humoral response, there was no obvious correlation between the cytokine profile observed and the subclasses of Ab induced.

L72 ANSWER 64 OF 64 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1988:155489 BIOSIS
DOCUMENT NUMBER: PREV198885079142; BA85:79142
TITLE: INCORPORATION OF THE MAJOR OUTER MEMBRANE PROTEIN OF NEISSERIA-GONORRHOEAE IN **SAPONIN-LIPID** COMPLEXES ISCOMS CHEMICAL ANALYSIS SOME STRUCTURAL FEATURES AND COMPARISON OF THEIR IMMUNOGENICITY WITH THREE OTHER ANTIGEN DELIVERY SYSTEMS.
AUTHOR(S): KERSTEN G F A [Reprint author]; TEERLINK T; DERKS H J G M; VERKLEIJ A J; VAN WEZEL T L; CROMMELIN D J A; BEUVERY E C
CORPORATE SOURCE: DEP INACTIVATED VIRAL VACCINES, NATL INST PUBLIC HEALTH ENVIRON HYG, PO BOX 1, 3720 BA BILTHOVEN, NETH
SOURCE: Infection and Immunity, (1988) Vol. 56, No. 2, pp. 432-438. CODEN: INFIBR. ISSN: 0019-9567.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 22 Mar 1988
Last Updated on STN: 22 Mar 1988

AB We incorporated the major outer membrane protein (PI) of Neisseria gonorrhoeae into immunostimulating complexes (iscoms) and examined some analytical, physicochemical, and **immunological** properties of these structures. The immunogenicity was compared with that of three other PI-containing structures, i.e., liposomes, outer membrane complexes produced by the bacterium, and protein-detergent-adjuvant complexes. AlPO4 and dioctadecyldimethylammonium bromide were used as adjuvants. Our results show that iscoms are much more immunogenic than liposomes and protein-detergent complexes but are also much more toxic. The localization of PI in iscoms was investigated. Therefore, the chymotrypsin susceptibility of PI in iscoms was tested, and the incorporation of fragments of PI was determined. Amphiphilic fragments of PI were incorporated in iscoms, but hydrophilic and hydrophobic fragments were not. Chymotrypsin degradation of PI in iscoms indicated that the protein is exposed to the environment in a similar manner as PI in outer membrane complexes, i.e., with both termini anchored in the iscom.

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